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TOXICOLOGICAL EVALUATION OF A BERYLLIUM MOTOR EXHAUST PRODUCT

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13 ABSTRACT A sample of an exhaust product collected from a beryllium-fueled NASA-JPL High Energy Upper Stage (HEUS) Motor has been evaluated for its physical and chemical characteristics and biological activity. The physical properties (surface area, crystallinity, average crystallite size, refractive index and density) of the "BeO exhaust product" more closely resemble those of the higher fired BeO samples than those of "active" BeO (calcined at 500 C). The sample is primarily BeO with low levels of impurities and low solubility. The biological activity was evaluated during a 100-week period following intratracheal administration of the "BeO exhaust product" to groups of rats in single doses of 50, 10, and 2 mg/kg. An additional group of rats received 50 mg/kg BeO calcined at 500 C as a positive control, and a final group received saline as a negative control. Histopathological examination 25, 50, 75 and 100 weeks following treatment revealed a pulmonary response to the "BeO exhaust product" less severe than that induced by the BeO calcined at 500 C, but with lesions similar in nature. Evaluation of tumorigenicity of the "BeO exhaust product" showed fewer tumors than were found in rats treated with the BeO calcined at 500 C. Studies on translocation of beryllium to extrapulmonary tissues (liver, kidney, spleen and bone), conducted 25 and 100 weeks following treatment, showed tissue levels of beryllium from 50 mg/kg "BeO exhaust product" to be lower than those from 50 mg/kg BeO calcined at 500 C. The beryllium concentrations in the tissues diminished with a decrease in dose of the "BeO exhaust product", and there were slight increases with length of time following treatment.

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SUMMARY

A sample of an exhaust product collected from a beryllium-fueled NASA-JPL High Energy Upper Stage (HEUS) Motor has been evaluated for its physical and chemical characteristics and biological activity. The characterization studies included surface area, crystallinity, average crystallite size, density, refractive index, solubility studies, trace elemental analysis, X-ray powder diffraction analysis, determination of carbon, hydrogen, chloride, oxygen and beryllium, particle size, and microscopy studies. Biological activity was evaluated by intratracheal administration of single doses of 50, 10, and 2 mg/kg of the "BeO exhaust product" to groups of rats, followed by a 100-week test period. Another group of rats received 50 mg/kg "active" BeO (calcined at 500 C) as a positive control, and a final group received saline as a negative control. Pathological examinations were conducted on groups of rats necropsied 25, 50, 75, and 100 weeks following treatment. Studies of the translocation of beryllium to extrapulmonary tissues (liver, kidney, spleen and bone) were conducted at 25 and 100 weeks.

The physical properties of the "BeO exhaust product" more closely resemble those of the higher fired BeO samples than those of "active" BeO (calcined at 500 C).

The surface area of the "BeO exhaust product" is slightly greater than that of the key BeO calcined at 1100 C, and density is midway between that of the key BeO calcined at 500 C and the density of the 1100 C material. The "BeO exhaust product" most closely resembles the key BeO calcined at 1600 C in average crystallite size and refractive index. It is slightly less crystalline than the key BeO samples calcined at 1100 and 1600 C. The sample is primarily BeO with low levels of impurities and low solubility.

Histopathological evaluation showed that the most severe pulmonary response was produced by the BeO calcined at 500 C. This reaction was a progressive proliferative response characterized in the earlier phases by fibrotic and epithelial metaplastic changes, advancing into neoplastic changes as indicated by the development of pulmonary carcinomas. The associated lymph nodes showed evidence of fibrotic proliferation.

The pulmonary lesions observed in the lungs of rats treated with 50 mg/kg "BeO exhaust product" were less severe than those induced by the key BeO calcined at 500 C, but were similar in nature. The severity of the pulmonary response diminished with a decrease in dose of the "BeO exhaust product", with only focal, minimal changes observed at the 2 mg/kg dose. No evidence of a proliferative response was observed in the associated lymph nodes from rats treated with even the highest dose of "Beo exhaust product".

The "BeO exhaust product" is also less active than the key BeO calcined at 500 C regarding tumorigenicity, with 25 rats treated with 50 mg/kg BeO calcined at 500 C developing primary pulmonary tumors, compared with 19 rats in the group treated with 50 mg/kg "BeO exhaust product". Only one pulmonary tumor was observed in the group of rats treated with 10 mg/kg "BeO exhaust product", and none in the 2 mg/kg treatment group developed pulmonary tumors. The tumors found in rats treated with 50 mg/kg "BeO exhaust product" also occurred later than those induced by the key BeO calcined at 500 C.

Studies on translocation of beryllium to extrapulmonary tissues showed tissue levels of beryllium from 50 mg/kg "BeO exhaust product" to be lower than those from 50 mg/kg "BeO calcined at 500 C. The beryllium concentrations in the tissues diminished with a decrease in dose of the "BeO exhaust product", and there were slight increases with length of time following treatment.

FOREWORD

This report was prepared by The Dow Chemical Company, Midland, Michigan 48640, under USAF Contract Number F-33615-70-1811. The work was administered under the direction of the Aerospace Medical Research Laboratory, Aerospace Medical Division, Air Force Systems Command, Wright-Patterson AFB, Ohio. Dr. Kenneth C. Back, Chief, Toxicology Branch, Toxic Hazards Division, was the Contract Monitor for the Aerospace Medical Research Laboratory. The work reported herein was conducted during the period from 1 July 1970 - 10 July 1972.

This project was carried out in the Chemical Biology Research Laboratory (formerly Biochemical Research Laboratory) by Dr. Howard C. Spencer, Principal Investigator, Mrs. Susan B. McCollister and Dr. Charles G. Humiston, Toxicologists, and Dr. R. J. Kociba, Veterinary Pathologist. Mr. C. E. Wade was responsible for animal supervision and for maintaining appropriate records. Dr. G. L. Sparschu, Veterinary Pathologist, made major contributions to the project through February 1972. Other major contributors are acknowledged at the end of the report.

This technical report has been reviewed and is approved.

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SECTION I

INTRODUCTION

The major toxicological portion of the beryllium propellant development program of the U. S. Air Force Rocket Propulsion Laboratories was performed by The Dow Chemical Company during the period from 1963-1968.(1)* Results of long-term studies on rats, injected intratracheally with well-characterized key samples of beryllium oxide prepared by calcining beryllium hydroxide for 10 hours at 500, 1100, and 1600 C, respectively, showed clearly that there is a definite gradation in biological response depending upon the oxide administered. Thus, the oxide calcined at 500 C was highly active as judged by histopathological examination of the lungs, incidence of tumors, and translocation of beryllium from the lungs to other tissues. In contrast, the oxide calcined at 1600 C showed less severe effects. Dose-response studies were carried out, using carefully prepared subsamples of "respirable particle size" of the three key oxides; results showed a definite gradation in response which diminshed with decreasing dosages of the administered oxide. Investigations on motor exhaust products have shown that most samples have chemical, physical, and toxicological properties similar to the beryllium oxide calcined at 1600 C. On the other hand, other samples were heterogeneous, contained considerable quantities of water-soluble beryllium and varied in toxicity.

*References in parentheses.

The latest research effort, conducted under Contract No. F 33615-70-0-1811 and reported herein, was designed to define the physical-chemical characteristics and toxicological properties of an exhaust product collected from a beryllium-fueled NASA-JPL High Energy Upper Stage (HEUS) Motor. This information will be used to help the U. S. Air Force medical authorities make judgment on the hazards associated with open air firings of beryllium-fueled rocket motors.

SECTION II

SAMPLE STUDIES

A. IDENTIFICATION OF TEST SAMPLES

1. "BeO Exhaust Product"

The exhaust product studied was received in three vials labeled as follows:

a. "High fired BeO-NASA HEUS Motor 22 Jan. 1970 Composite from SP65-1417 #5"

b. "NASA HEUS Motor - High fired BeO Composite SP65-4132 #1"

c. "High fired BeO NASA HEUS Motor 22 Jan. 1970 Composite from SP65-1287 #9"

The contents from these three vials were combined into one sample totaling 104g. This sample is hereafter identified as "BeO exhaust product".

2. BeO Calcined at 500 C ("Active" BeO)

This sample was previously investigated in the Dosage-Response Study of the earlier contract (AF33[615]-3842). It is of known physical-chemical properties and biological activity and was included in this study as a positive control.

B. PHYSICAL AND CHEMICAL CHARACTERIZATION STUDIES

1. Methods

a. "BeO Exhaust Product"

The characterization studies conducted on the "BeO exhaust product", together with the analytical techniques employed, are given below:

Specific surface area - nitrogen adsorption.

Average crystallite size - X-ray diffraction.

Crystallinity - polarized light microscopy.

Refractive index - dispersion staining.

Density - sink-float method.

Major components of sample - X-ray powder diffraction.

Trace elements in sample - emission spectroscopy and X-ray fluorescence.

Sample solubility - A 1% aqueous suspension of sample was agitated for 16 hours at room temperature, followed by filtration through a 0.45 μ Millipore filter. The precipitate was dried and weighed to determine total sample solubility.

Determination of major and trace components in soluble and insoluble fractions from sample solubility studies - X-ray powder diffraction and emission spectroscopy.

Determination of amount of beryllium soluble in water - 0.1 g sample shaken in 45 ml water at room temperature for 35 hours, followed by filtration through a 0.45 μ Millipore filter; analysis of filtrate for beryllium by emission spectroscopy.

Determination of amount of beryllium soluble in 0.1N HCl- 30 mg sample in 50 ml 0.1N HCL allowed to stand 1 hour at room temperature, then filtered through a 0.45 μ Millipore filter; analysis of filtrate for beryllium by emission spectroscopy.

Determination of amount of beryllium soluble in 6N HCl - 30 mg sample in 7.5 ml 6N HCl allowed to stand 30 minutes at room temperature, then filtered through a 0.45 μ Millipore filter; analysis of filtrate by emission spectroscopy.

Elemental analysis -
beryllium by gravimetric method
carbon by microcombustion method
hydrogen by microcombustion method
oxygen by neutron activation
chloride by microvolumetric method

Particle characterization -
light microscopy
transmission electron microscopy
scanning electron microscopy

Particle size -
Microscopy and Coulter Counter technique.

b. BeO Calcined at 500 C

The physical and chemical properties of this sample were investigated in detail under Contract No. AF33[615]-3842, using the techniques described above(1).

2. Results

Physical properties of the "BeO exhaust product" are presented in Table I. Data on key samples of BeO calcined at 500, 1100, and 1600 C, studied and reported under the previous contract (1), are included for comparative purposes. Surface area of the "BeO exhaust product" is slightly greater than that of the key BeO calcined at 1100 C, and density is midway between that of the key BeO calcined at 500 C and the density of the 1100 C material. The "BeO exhaust product" most closely resembles the key BeO calcined at 1600 C in average crystallite size and refractive index. It is slightly less crystalline than the key BeO samples calcined at 1100 and 1600 C.

Trace elements in the total sample of "BeO exhaust product" are presented in Table II and the sample components identified by X-ray powder diffraction are given

in Table III. Sample solubility studies showed that only 0.71% of the total sample is soluble. Analysis of the soluble and insoluble fractions by X-ray powder diffraction are also presented in Table III, and trace elemental analyses are reported in Table IV. The results were unremarkable.

Results of studies to determine the water and acid solubility of beryllium in the sample are presented in Table V. The water and acid soluble beryllium in this sample are extremely low.

Results of elemental analyses are presented in Table VI. Particle size distribution, as determined by the Coulter Counter, is given in Table VII. Results showed that approximately 87% of the sample mass was composed of particles less than 11μ in diameter. Particle size distribution measured on photomicrographs using a Zeiss Counter showed 94% of the particles to be less than 5μ in diameter.

Photomicrographs of the "BeO exhaust product" at several magnifications utilizing light and electron microscopy are shown in Figures 1-10. The crystalline nature of the material is evident in Figures 1 and 3. Figure 2 (same field as Figure 1) shows the dark particles that did not appear to be crystalline. It is apparent in the photomicrographs that most of the particles were less

than 5μ in diameter. Figures 9 and 10, taken with the Steroscan Electron Microscope, show the presence of numerous fine particles attached to the larger particles of the sample.

SECTION III

ANIMAL STUDIES

A. EXPERIMENTAL

1. Test Animals and Maintenance

Sprague-Dawley (Spartan strain) female rats were employed in this study. They were 8 weeks old and averaged 200g in body weight at time of treatment. The rats were specific pathogen free-derived but were maintained in conventional facilities during the study. They were housed singly in wire-bottom cages and had access to food and water *ad libitum*. The basic ration was pelletized Purina laboratory chow.

2. Experimental Design and Sample Administration

The sample was administered intratracheally as a saline suspension to groups of 60 rats each at doses of 50, 10, or 2 mg/kg body weight. A modification of the self-retaining illuminated laryngoscopic speculum, developed by Dr. Paul Gross of the Industrial Hygiene Foundation, Mellon Institute, was used for sample administration(2), each rat receiving 1.0cc of the suspension in a concentration calculated to yield the appropriate dose. An additional 60 rats received 50 mg/kg "active" BeO (calcined at 500 C). A group of 60 rats received 1.0 cc saline to serve as controls. A total of 300 rats were started on experiment. The experimental design is presented in Table VIII.

3. Parameters Evaluated

a. Appearance and demeanor - The rats were observed frequently for any changes in appearance and demeanor.

b. Mortality - Records of mortality were maintained. Rats which died during the course of the study or were considered moribund were subjected to pathological examination.

c. Body weights - The rats were weighed weekly for the first 3 months and biweekly thereafter.

d. Pathology - Scheduled necropsy examinations were conducted 25, 50, 75 and 100 weeks after the single intratracheal administration of the test materials.

Test Material and Dose	Number of Rats Necropsied			
	25 Weeks	50 Weeks	75 Weeks	100 Weeks
"BeO Exhaust Product",50 mg/kg	10	10	10	10
"BeO Exhaust Product",10 mg/kg	10	10	10	15
"BeO Exhaust Product",2 mg/kg	10	10	10	8
BeO Calcined at 500 C, 50 mg/kg	10	10	10	5
Control,Saline 1 ml	10	10	10	11

At each of the scheduled necropsies, the rats were starved overnight and killed by decapitation. Prior to decapitation, each rat was anesthetized with methoxyflurane and the trachea clamped. Each rat was subjected to a complete gross examination and the brain, spleen

heart, liver and kidneys were weighed. The lungs of each rat were distended with buffered 10% formalin under a pressure of 12 cm prior to preservation in formalin fixative. Specimens of mediastinal lymph nodes, heart, spleen, brain, liver, kidney, ovary and any nodules or masses suggestive of tumor development or other pathologic processes were also preserved in buffered 10% formalin at each of the scheduled necropsies.

Histopathological examinations were conducted on sections of lungs and mediastinal lymph nodes from rats at each of the interim kills (25, 50, and 75 weeks). At the final necropsy (100 weeks), histopathological examination was extended to also include sections of the liver, kidney, spleen, heart, and brain as well as any other tissue specimens suggestive of tumor development or other pathologic process. In all cases, routine histologic procedures were used to prepare paraffin embedded sections (5-6μ) stained with hematoxylin and eosin. Selected lung and mediastinal lymph node sections were also stained with Gordon and Sweets' silver impregnation procedure for evaluation of reticulum content.

All rats that died spontaneously or were sacrificed in a moribund condition prior to completion of the scheduled 100 week observation period were subjected

to a gross and histopathological examination for evidence of pulmonary changes or other significant pathologic lesions in other tissues.

e) Translocation of beryllium to extrapulmonary tissues - Portions of liver, kidney, spleen and bone were obtained from all rats necropsied 25 and 100 weeks following treatment. These 4 tissues from 4 rats per treatment group were analyzed for beryllium by emission spectroscopy.

B. RESULTS

1. Appearance and demeanor

None of the rats exhibited any changes in appearance and demeanor that could be associated with treatment.

2. Mortality (Table IX)

Mortality was similar for the groups receiving the various doses of "BeO exhaust product" and the saline controls, while mortality was slightly increased in the group of rats receiving the key BeO calcined at 500 C. This increase in mortality with the "active" material has been observed and reported in earlier work (1).

3. Body Weights (Figure 11)

Body weight gains were comparable for the groups of rats treated with the various doses of "BeO exhaust product" and the saline control group. The group of rats treated with 50 mg/kg BeO calcined at 500 C showed mean body weights consistently lower than the controls and other test groups throughout the study.

4. Pathology

a. Organ Weight Data (Tables X-XIII)

No treatment-related differences in organ weights were noted.

b. Gross and Histopathologic Examination

1) Interim Necropsy at 25 Weeks (Table XIV)

a) Saline Control - There were no gross lesions in the lungs or associated lymph nodes. Histologic change was limited to one focus of alveolar epithelialization observed in the lung of 1/10 rats.

b) "BeO Exhaust Product" - Grossly, 10/10 rats in the 50 mg/kg group, 5/10 rats at 10 mg/kg and none in the 2 mg/kg group, had multifocal areas of pulmonary consolidation. One rat at 50 mg/kg had enlarged mediastinal lymph nodes.

Histologically, within the 50 mg/kg treatment group the lungs had multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, polymorphonuclear leukocytes and translucent aggregates assumed to be the test material. Multifocal areas of alveolar epithelialization were present in all rats, with squamous metaplasia in one rat and focal necrosis of alveolar walls in two rats.

Histologically, the lungs of the rats receiving 10 mg/kg of "BeO exhaust product" showed changes similar to those receiving 50 mg/kg with the exception that the changes tended to be more focal and less severe, and there was no evidence of squamous metaplasia or focal necrosis of alveolar walls.

In rats receiving 2 mg/kg "BeO exhaust product", the vast majority of the lung tissue was entirely normal. The very minimal and focal changes that were present were similar to those changes observed in rats receiving 10 mg/kg "BeO exhaust product".

Histologic examination of the associated lymph nodes revealed no evidence of a proliferative response in spite of the fact that aggregates of test material were present in lymph nodes at all three dosage levels (quantities dependent on dosage).

c) BeO Calcined at 500 C - Grossly, all rats showed multifocal areas of pulmonary consolidation and enlarged associated lymph nodes.

Histologically, the typical lung reaction observed in all rats included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, polymorphonuclear leukocytes, translucent aggregates

assumed to be BeO test material, multifocal areas of alveolar epithelialization and necrosis of alveolar walls. Squamous metaplasia was noted in 2/10 rats and focal septal fibrosis in 1/10 rats.

The associated lymph nodes had aggregates of BeO test material accompanied by a proliferative response, with deposition of fibrotic tissue.

2) Interim Necropsy at 50 Weeks (Table XV)

a) Saline Control - There were no gross or microscopic lesions observed in the lungs or associated lymph nodes.

b) "BeO Exhaust Product" - Grossly, all rats in the 50 mg/kg group and 8/10 in the 10 mg/kg group showed multifocal areas of pulmonary consolidation. The consolidated foci in the 10 mg/kg treatment group were not as diffuse or numerous as those observed in the 50 mg/kg level. No rat in the 2 mg/kg group had gross evidence of pulmonary consolidation.

Eight of the 10 rats at 50 mg/kg had minimal enlargement of the associated lymph nodes. No lymph node enlargement was observed in the 10 or 2 mg/kg treatment groups.

Histologically, the lungs of rats from the 50 mg/kg treatment groups showed all the changes which were noted after 25 weeks. In addition,

the epithelial metaplastic changes appeared to be more advanced, with evidence of squamous metaplasia and keratin formation observed in lungs of all rats after 50 weeks.

In the group that had received 10 mg/kg "BeO exhaust product", the lung changes were similar to those noted after 25 weeks. In addition, one rat showed histologic evidence of squamous metaplasia with keratin formation. Rats that had received 2 mg/kg "BeO exhaust product" showed lung changes similar to those noted previously after 25 weeks.

Histologic examination of the associated lymph nodes revealed no evidence of a proliferative response in spite of the fact that aggregates of test material were present in lymph nodes at all three dosage levels of "BeO exhaust product" (quantities dependent on dosage).

c) BeO Calcined at 500 C - Gross examination revealed all rats to have multifocal areas of pulmonary consolidation and enlargement of the associated lymph nodes.

Histologically, the lungs showed all the changes which were noted after 25 weeks. In addition, epithelial metaplastic changes were now more advanced, with squamous metaplasia

and keratin formation present in lungs of all the rats. The lungs of two rats also had focal septal fibrosis. The associated lymph nodes had aggregates of BeO test material accompanied by a proliferative response, with deposition of fibrotic tissue.

3) Interim Necropsy at 75 Weeks (Table XVI)

a) Saline Control - Gross and microscopic changes in the lungs and associated lymph nodes were limited to several small accumulations of inflammatory cells in the lungs of three rats.

b) "BeO Exhaust Product" - Grossly, all 10 rats in the 50 mg/kg group showed multifocal areas of pulmonary consolidation, and the associated lymph nodes were enlarged. Multifocal areas of consolidation were present to a lesser degree in the lungs of all rats in the 10 mg/kg group and the associated lymph nodes were enlarged. In the 2 mg/kg group, minimal focal pulmonary consolidation was limited to 4/10 of the rats, and the associated lymph nodes were not increased in size.

Histologically, the lungs of rats from the 50 mg/kg treatment group showed all the changes noted after 25 and 50 weeks. In addition, metaplastic, fibrotic and neoplastic changes were

common, with areas of squamous metaplasia and keratin formation in 10/10 rats. Primary pulmonary carcinomas were observed in 4/10 rats and primary pulmonary adenoma formation occurred in 1/10 rats.

In the 10 mg/kg treatment group, all changes observed after 25 and 50 weeks were also noted after 75 weeks. However, the lungs of 2/10 rats now had areas of squamous metaplasia with keratin formation and 1/10 rats had a focal proliferative area diagnosed as primary pulmonary carcinoma. In rats treated with 2 mg/kg "BeO exhaust product" the lung changes did not differ significantly from the minimal focal lesions observed after 25 and 50 weeks.

Histologic examination of the associated lymph nodes again revealed no evidence of a proliferative response at any of the 3 dosage levels of "BeO exhaust product". Aggregates of test material were present in the lymph nodes (quantities dependent on dosage).

c) BeO Calcined at 500 C - Gross examination revealed multifocal areas of pulmonary consolidation and enlargement of the associated lymph nodes in all rats.

Histologically, the lungs showed all the changes seen previously after 25 and 50 weeks. In addition, metaplastic changes were common, with all lungs containing areas of adenomatoid change, alveolar septal fibrosis and squamous metaplasia with keratin formation. Five out of 10 rats had primary pulmonary carcinomas and one rat showed primary pulmonary adenoma formation.

The associated lymph nodes had aggregates of the test material accompanied by a proliferative response, with deposition of fibrotic tissue.

4) Final Necropsy at 100 Weeks - Pulmonary System (Table XVII)

a) Saline Control - Gross and microscopic changes in the lungs and associated lymph nodes were limited to very minimal accumulations of inflammatory cells and material in the lungs of 4/11 rats.

b) "BeO Exhaust Product" - Grossly, all 10/10 rats in the 50 mg/kg treatment group showed areas of pulmonary consolidation, and the associated lymph nodes were enlarged.

In the 10 mg/kg treatment group, a lesser degree of pulmonary consolidation, along with lymph node enlargement, was noted in 14/15 rats.

In the 2 mg/kg treatment group, gross changes were limited to minimal focal areas of pulmonary consolidation in 2/8 rats, with no enlargement of associated lymph nodes.

Histologically, the lungs of all rats treated with 50 mg/kg "BeO exhaust product" showed those changes noted at the earlier interim necropsies . However, the metaplastic, fibrotic and neoplastic changes were now more common, with lungs of 10/10 rats containing areas of septal fibrosis associated with adenomatous and adenomatoid changes. Primary pulmonary carcinomas were noted in 9/10 rats.

In the 10 mg/kg treatment group, the histologic changes were similar to those observed previously at the 75-week necropsy, except that focal alveolar metaplasia and focal septal fibrosis were now more commonly observed. No primary pulmonary tumors were diagnosed in this group at the 100-week necropsy.

In rats that had received 2 mg/kg "BeO exhaust product", the lung changes were essentially the same as those observed previously after 75 weeks. Additional changes included minimal focal septal fibrosis observed

occasionally in all rats and one isolated focus of squamous metaplasia in 1/8 rats that were necropsied after 100 weeks.

Histologic examination of the associated lymph nodes again revealed no evidence of a proliferative response at any of the three dosage levels of "BeO exhaust product". Aggregates of test material were present (quantities dependent on dosage).

c) BeO Calcined at 500 C - Gross examination revealed 5/5 rats to have multifocal areas of pulmonary consolidation and enlargement of the associated lymph nodes.

Histologically, the lungs showed all the changes noted at the earlier necropsies. Areas of alveolar metaplasia, visible as adenomatous and adenomatoid change associated with septal fibrosis, occurred in all lungs. Primary pulmonary carcinomas occurred in all (5/5) rats.

The associated lymph nodes had aggregates of test material accompanied by proliferative response, with deposition of fibrotic tissue.

5) Final Necropsy at 100 Weeks - Nonpulmonary Major Organs (Tables XVIII and XIX)

Gross and microscopic examination of major nonpulmonary organs of rats necropsied after 100

weeks revealed a variety of inflammatory, degenerative and proliferative lesions in both control and treated groups.

Most of the lesions noted were similar to those listed by Cotchin and Roe as spontaneous occurrences in aged rats (3). These nonpulmonary lesions were not considered to be related to administration of the various test materials.

Various nonpulmonary tumors occurred in the various treatment and control groups, with no evidence to suggest a relationship to treatment with the test materials.

6) Spontaneous Deaths (Tables XX through XXIV)

Gross and microscopic examination of all rats that died spontaneously (or were sacrificed in a moribund condition) revealed some lesions considered spontaneous in nature and also some lesions considered related to administration of the test materials. Those lesions considered related to treatment closely resembled the pulmonary lesions noted upon examination of similarly treated rats at the scheduled necropsies.

Those lesions considered spontaneous in nature occurred in both control and treated rats. The most common spontaneous lesions included pituitary and mammary tumors, varying degrees of chronic nephritis and focal myocardial degenerative changes.

7) Summation of Primary Pulmonary Tumors (Tables (XXV-XXVIII)

All primary pulmonary tumors were of epithelial origin, with the vast majority possessing morphological characteristics of carcinomas. Metastatic carcinoma cells were sometimes observed in the associated lymph nodes. In a few instances the tumor morphology in a lung was more characteristic of adenoma formation.

The occurrence of primary pulmonary tumors in the various treatment groups is presented in Tables XXV, XXVI and XXVII. The earliest primary pulmonary tumor was noted 58 weeks following treatment in the group of rats that had received 50 mg/kg BeO calcined at 500 C, so the tabulation was started at that point (Table XXV). For comparative purposes, 58 weeks was used as the starting time in tabulation of tumors in the other groups, although the first tumor was not noted in the group receiving 50 mg/kg "BeO exhaust product" until the 75 week necropsy. The tabulations show a higher occurrence of tumors in the group of rats treated with 50 mg/kg BeO calcined at 500 C than was found at the same dose of the "BeO exhaust product".

Table XXVIII summarizes the distribution according to time periods of the pulmonary tumors found in the various treatment groups.

5. Translocation of beryllium to extrapulmonary tissues (Tables XXIX-XXX).

Twenty-five weeks following treatment, beryllium was measurable in liver, kidney, spleen and bone from rats receiving 50 mg/kg "BeO exhaust product", while only liver and spleen showed detectable quantities at the 10 mg/kg dose. Tissue from rats receiving the 2 mg/kg dose showed no measurable quantities of beryllium. Levels of beryllium in tissues from rats treated with 50 mg/kg BeO calcined at 500 C were higher than those found in rats treated with the same dose of "BeO exhaust product".

Levels of beryllium in tissues 100 weeks following treatment with "BeO exhaust product" were generally slightly increased over the 25-week values, although there was still no detectable beryllium in kidney and bone at the 10 and 2 mg/kg doses. Again, the data show that translocation of beryllium to extrapulmonary tissues following intratracheal injection of "BeO exhaust product" is of a lower order than the translocation following administration of BeO calcined at 500 C.

SECTION IV

SUMMARY

A sample of an exhaust product collected from a beryllium-fueled NASA-JPL High Energy Upper Stage (HEUS) Motor has been evaluated for its physical and chemical characteristics and biological activity. The characterization studies included surface area, crystallinity, average crystallite size, density, refractive index, solubility studies, trace elemental analysis, X-ray powder diffraction analysis, determination of carbon, hydrogen, chloride, oxygen and beryllium, particle size, and microscopy studies. Biological activity was evaluated by intratracheal administration of single doses of 50, 10, and 2 mg/kg of the "BeO exhaust product" to groups of rats, followed by a 100-week test period. Another group of rats received 50 mg/kg "active" BeO (calcined at 500 C) as a positive control, and a final group received saline as a negative control. Pathological examinations were conducted on groups of rats necropsied 25, 50, 75, and 100 weeks following treatment. Studies of the translocation of beryllium to extrapulmonary tissues (liver, kidney, spleen and bone) were conducted at 25 and 100 weeks.

The physical properties of the "BeO exhaust product" more closely resemble those of the higher fired BeO samples than those of "active" BeO (calcined at 500 C).

The surface area of the "BeO exhaust product" is slightly greater than that of the key BeO calcined at 1100 C, and density is midway between that of the key BeO calcined at 500 C and the density of the 1100 C material. The "BeO exhaust product" most closely resembles the key BeO calcined at 1600 C in average crystallite size and refractive index. It is slightly less crystalline than the key BeO samples calcined at 1100 and 1600 C. The sample is primarily BeO with low levels of impurities and low solubility.

Histopathological evaluation showed that the most severe pulmonary response was produced by the BeO calcined at 500 C. This reaction was a progressive proliferative response characterized in the earlier phases by fibrotic and epithelial metaplastic changes, advancing into neoplastic changes as indicated by the development of pulmonary carcinomas. The associated lymph nodes showed evidence of fibrotic proliferation.

The pulmonary lesions observed in the lungs of rats treated with 50 mg/kg "BeO exhaust product" were less severe than those induced by the key BeO calcined at 500 C, but were similar in nature. The severity of the pulmonary response diminished with a decrease in dose of the "BeO exhaust product", with only focal, minimal changes observed at the 2 mg/kg dose. No evidence of a proliferative response was observed in the associated lymph nodes from rats treated with even the highest dose of "Beo exhaust product".

The "BeO exhaust product" is also less active than the key BeO calcined at 500 C regarding tumorigenicity, with 25 rats treated with 50 mg/kg BeO calcined at 500 C developing primary pulmonary tumors, compared with 19 rats in the group treated with 50 mg/kg "BeO exhaust product". Only one pulmonary tumor was observed in the group of rats treated with 10 mg/kg "BeO exhaust product", and none in the 2 mg/kg treatment group developed pulmonary tumors. The tumors found in rats treated with 50 mg/kg "BeO exhaust product" also occurred later than those induced by the key BeO calcined at 500 C.

Studies on translocation of beryllium to extrapulmonary tissues showed tissue levels of beryllium from 50 mg/kg "BeO exhaust product" to be lower than those from 50 mg/kg "BeO calcined at 500 C. The beryllium concentrations in the tissues diminished with a decrease in dose of the "BeO exhaust product", and there were slight increases with length of time following treatment.

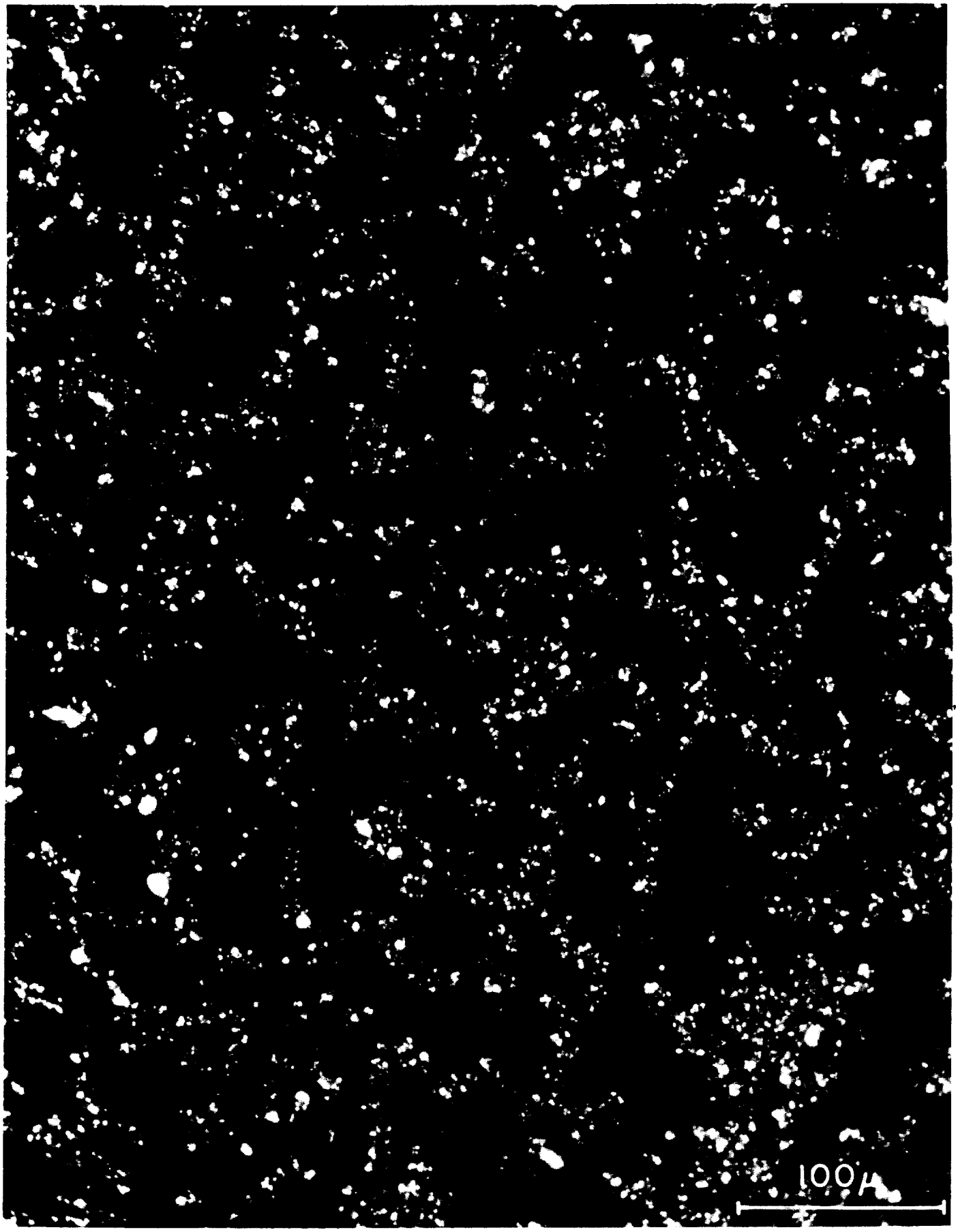

Figure 1. Light photomicrograph of "BeO exhaust product" (polarized light). x 400.

Figure 2. Light photomicrograph of "BeO exhaust product" (same field as Figure 1). x 400

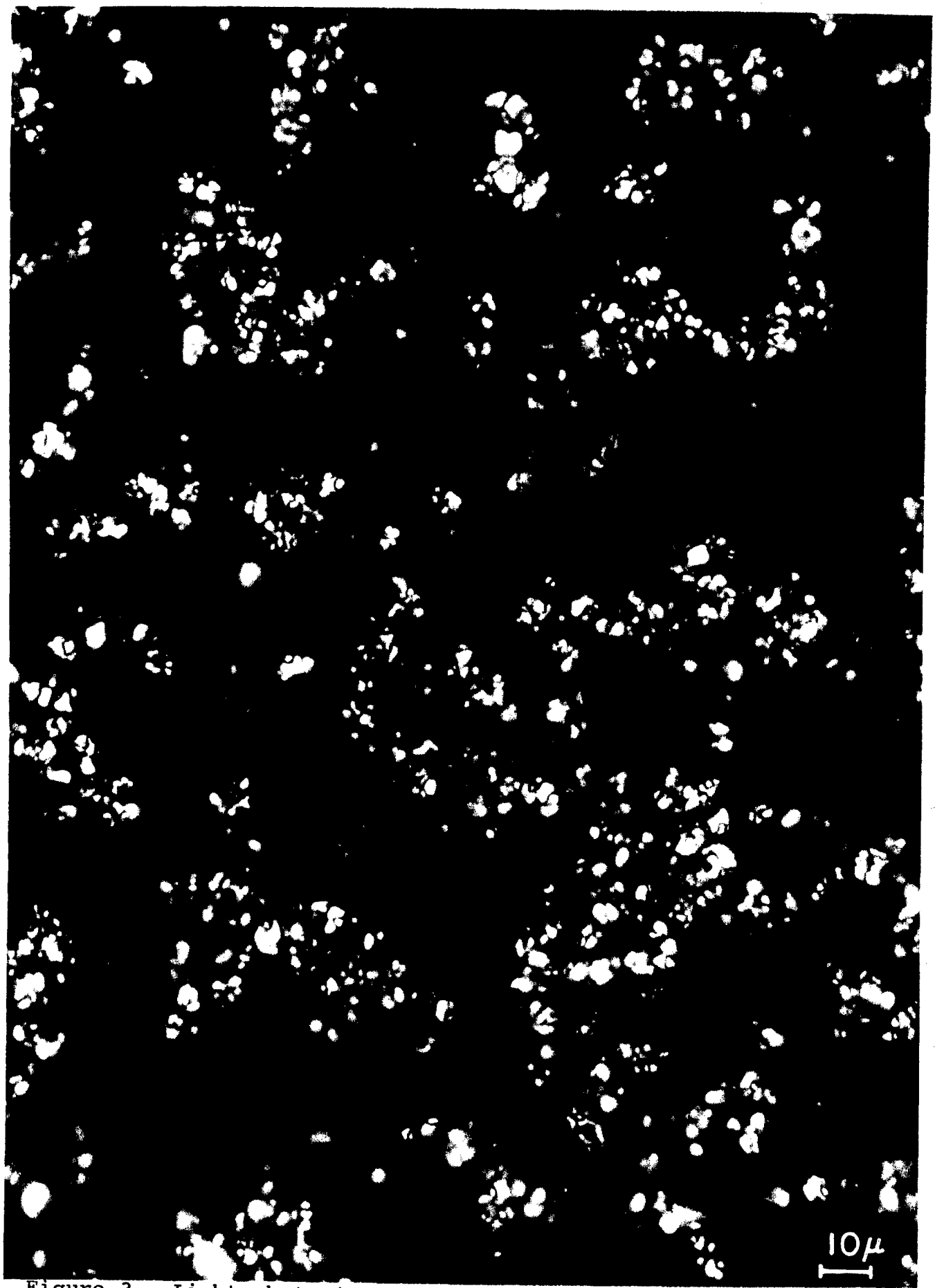

Figure 3. Light photomicrograph of "BeO exhaust product" (polarized light). x 1000

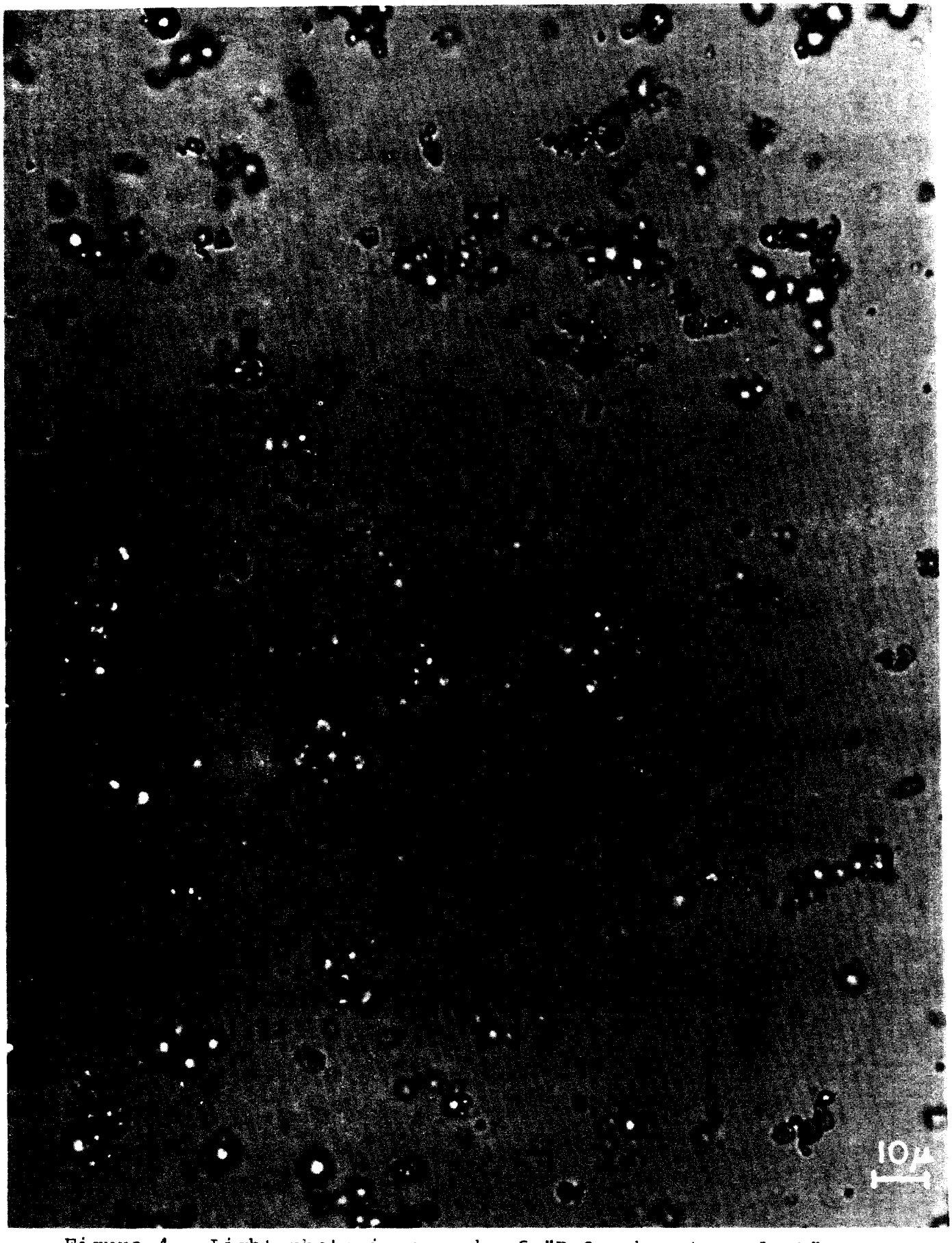

Figure 4. Light photomicrograph of "BeO exhaust product". x 1000.

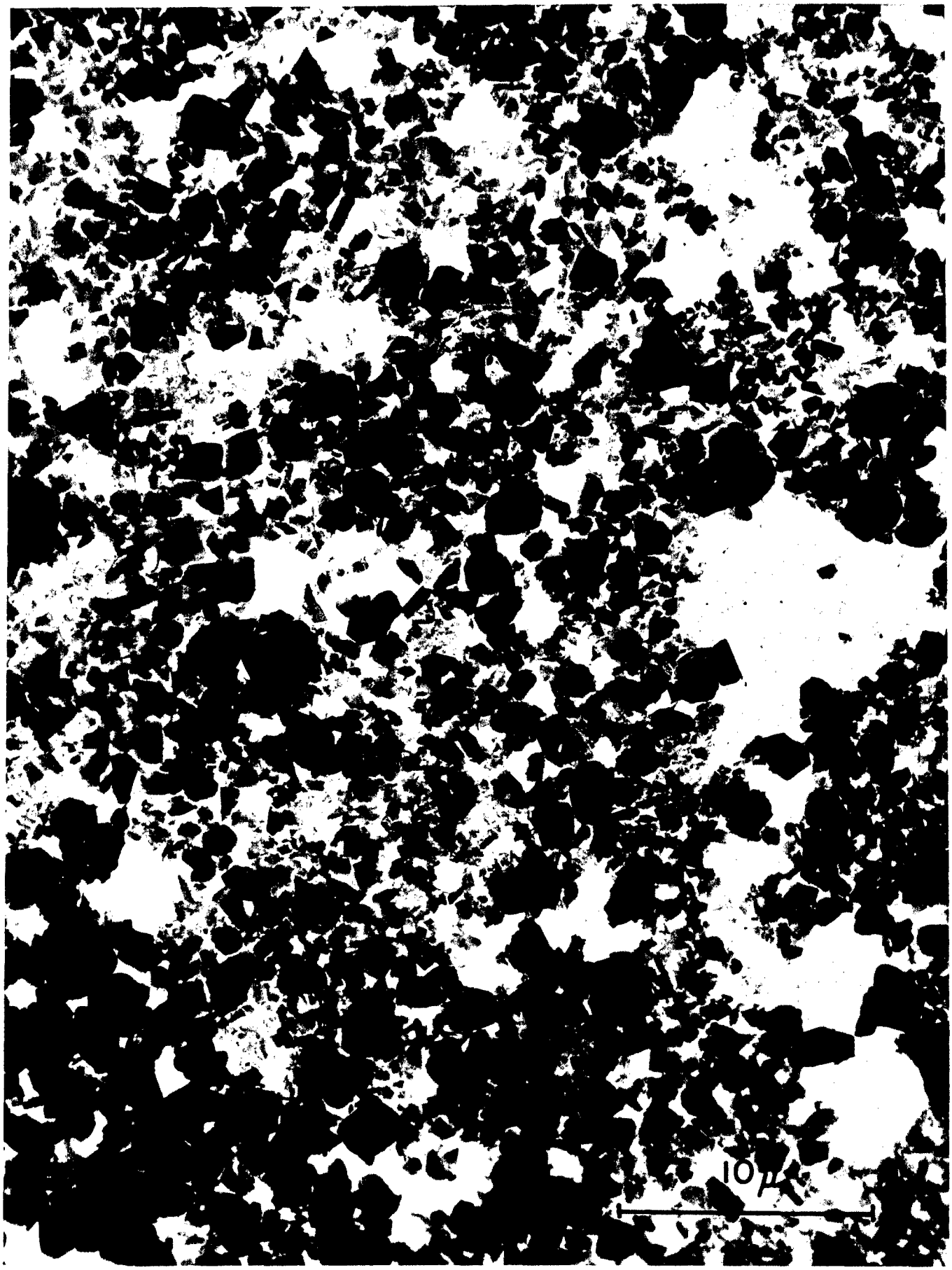

Figure 5. Electron photomicrograph of "BeO exhaust product". x 4800.

Figure 6. Electron photomicrograph of "BeO exhaust product". x 13,500.

Figure 7. Electron photomicrograph of "BeO exhaust product". x 25,500

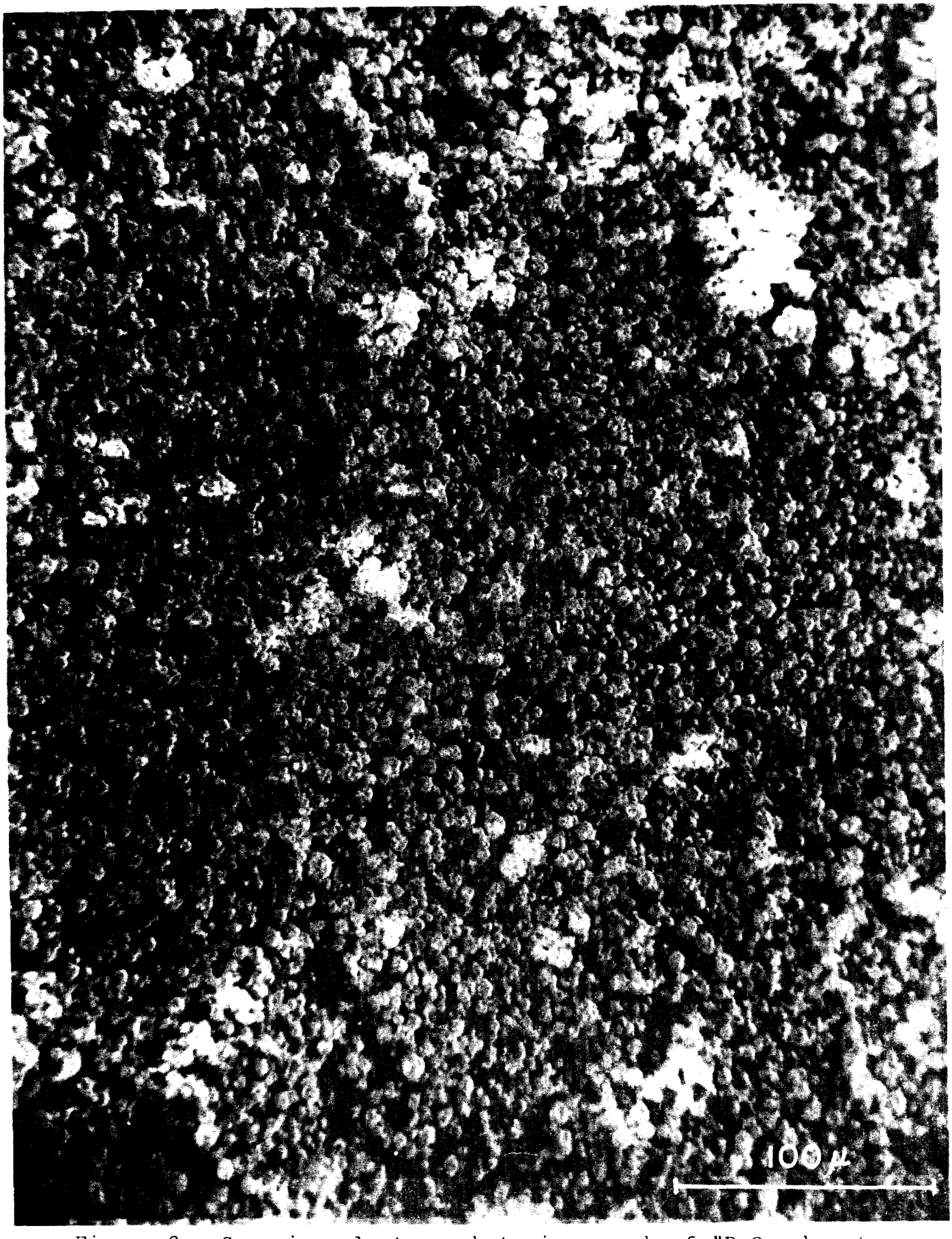

Figure 8. Scanning electron photomicrograph of "BeO exhaust product". x 500

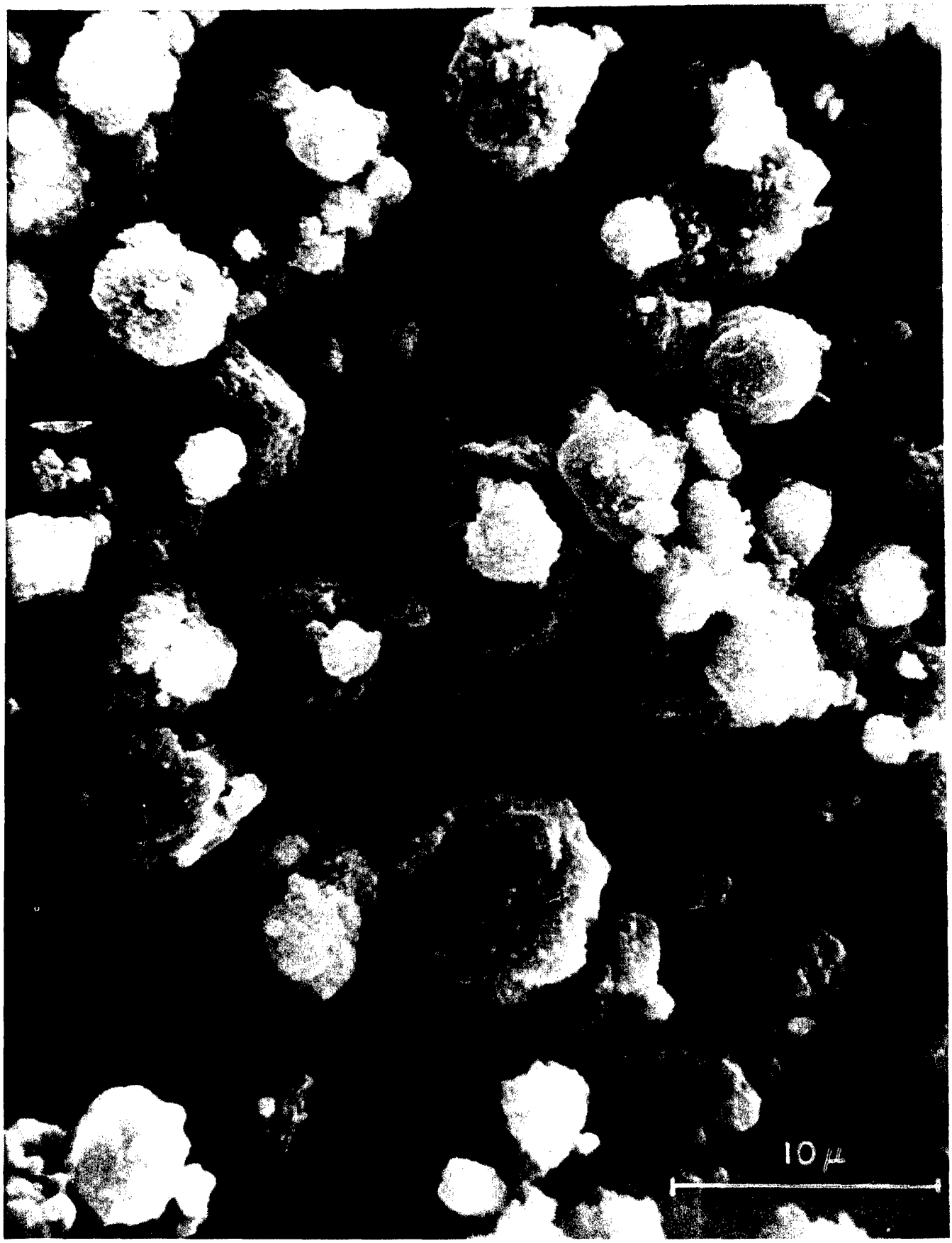

Figure 9. Scanning electron photomicrograph of "BeO exhaust product". x 5000.

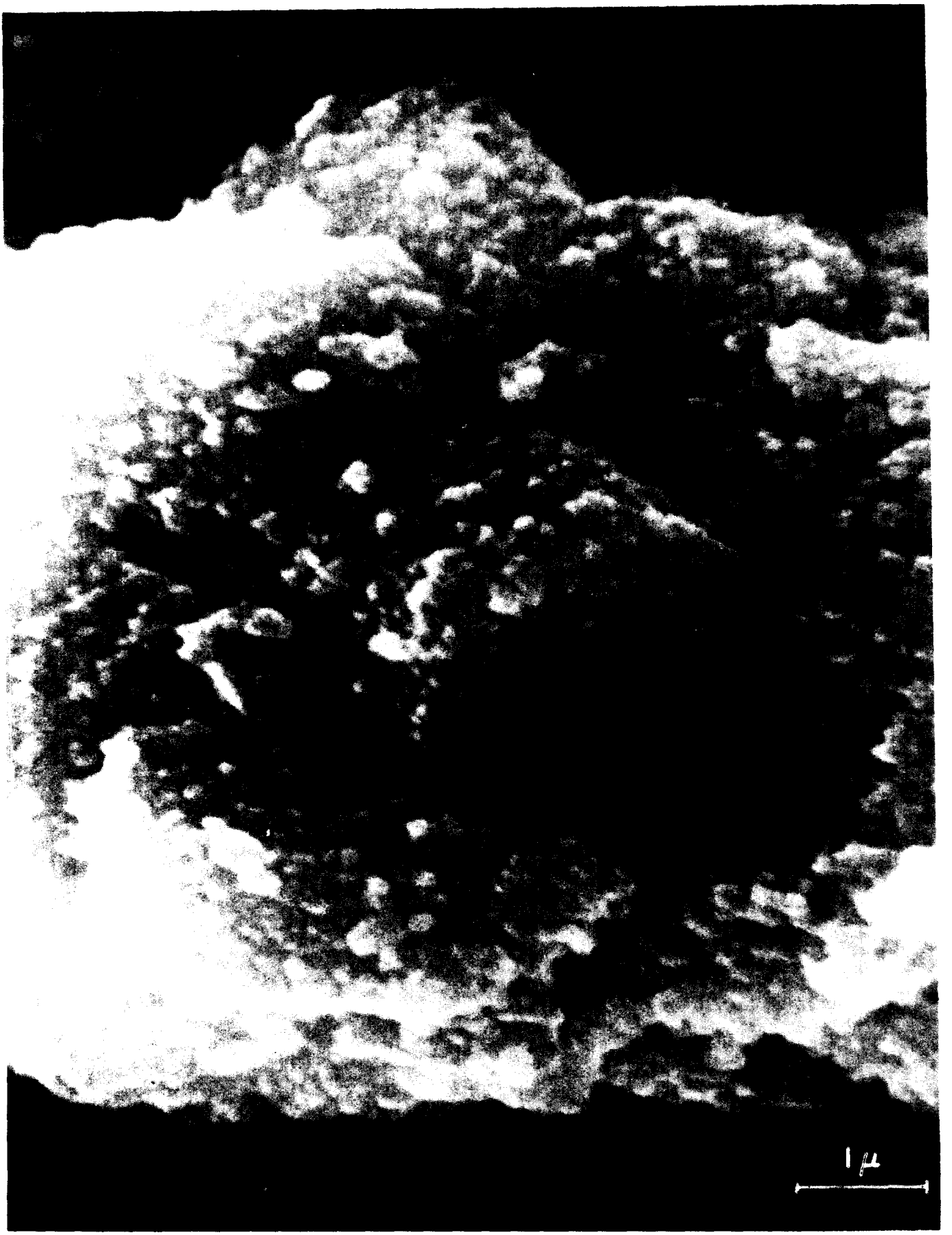

Figure 10. Scanning electron photomicrograph of "BeO exhaust product". x 25,000.

FIGURE 11

BODY WEIGHT CURVES FOR FEMALE RATS 100 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF BeO EXHAUST PRODUCT

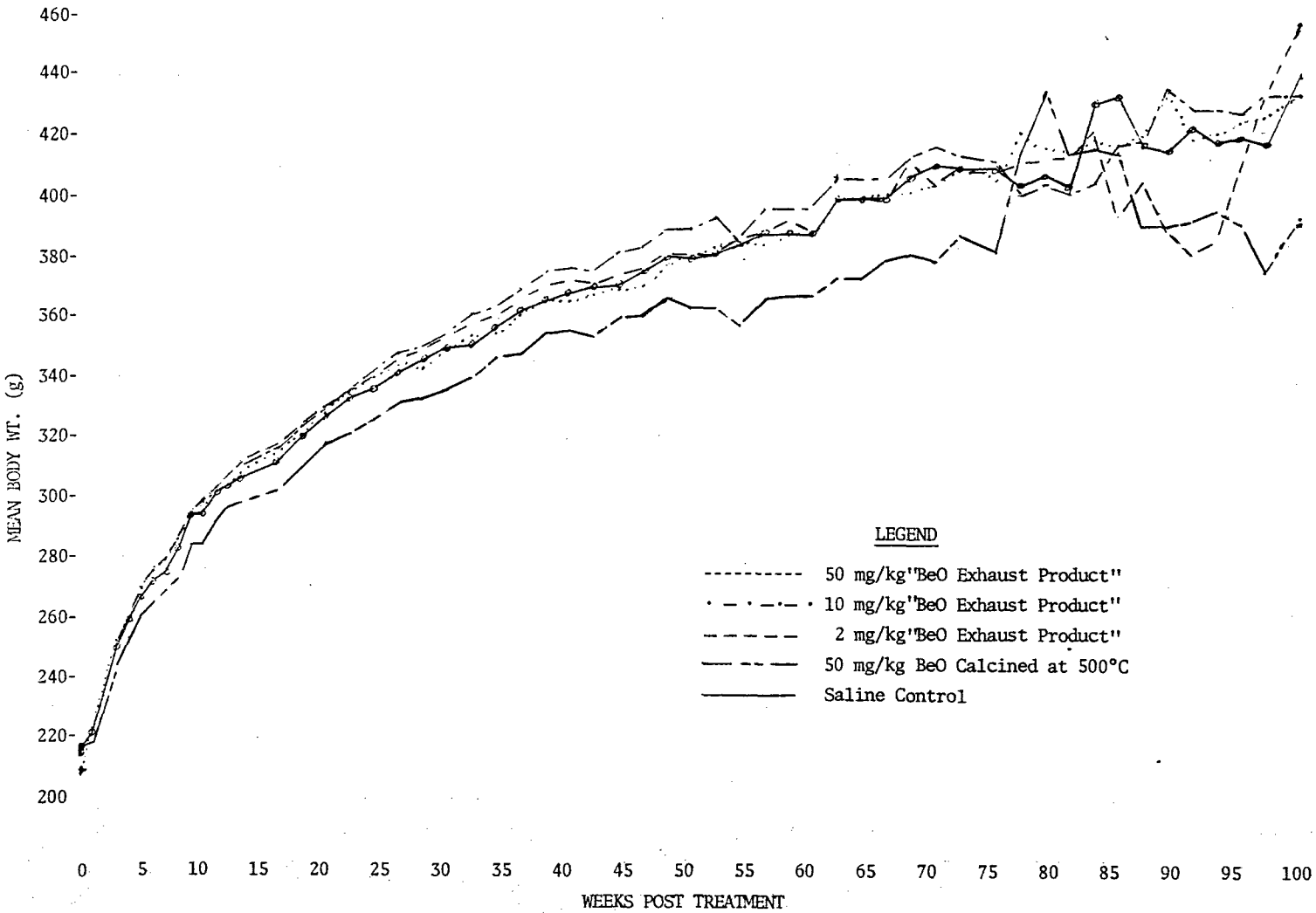

TABLE I

PHYSICAL PROPERTIES OF "BeO EXHAUST PRODUCT" COMPARED WITH KEY SAMPLES OF BeO

Property	BeO Calcined for 10 hours at: 500 C	1100 C	1600 C	"BeO Exhaust Product"
Specific Surface Area m^2/g	50.8	2.2	1.3	2.51
Average Crystallite Size Å	150	1500	1600	2000 ± 300
Crystallinity %	< 10	100	100	95
Refractive Index	1.683 ± 0.003	1.704 ± 0.002	1.711 ± 0.007	1.712 ± 0.002
Density g/ml	2.87 ± 0.07	2.98 ± 0.02	3.00 ± 0.03	2.92 ± 0.03

TABLE II

ANALYSIS FOR TRACE ELEMENTS BY EMISSION SPECTROSCOPY AND X-RAY FLUORESCENCE IN "BeO EXHAUST PRODUCT"

Element	Percent (%) in Total Sample	
	Emission Spectroscopy	X-Ray Fluorescence
Al	0.005	-----
Ba	<0.001	-----
B	0.001-0.01	-----
Ca	0.7	1.1
Cd	<0.01	-----
Cl	-----	0.08
Co	<0.001	-----
Cu	0.001	-----
Cr	0.05	0.27
Fe	0.08	0.35
Mg	0.3	-----
Mn	0.005	0.015
Mo	<0.001	-----
Ni	<0.005	0.03
P	<0.1	-----
Pb	0.001-0.01	0.04
S	-----	0.04
Si	0.4	0.55
Sn	0.001	-----
Sr	Trace	0.03
Na	0.1-0.1	-----
Ti	0.08	0.08
V	<0.001	-----
Zn	0.01-0.1	0.18

TABLE III

X-RAY POWDER DIFFRACTION ANALYSIS OF
"BeO EXHAUST PRODUCT"

Sample	Components
Total Sample	BeO - Chief component $CaCO_3$ - Trace
Water-Soluble portion* (0.71% of sample is soluble)	$CaSO_4 \cdot 1/2H_2O$ Unidentified phase (May be a hydrated calcium silicate)
Water-Insoluble portion*	BeO

* After 16 hours of shaking a 1% suspension in water, at room temperature, and filtration through a 0.45μ millipore filter.

TABLE IV

ANALYSIS FOR TRACE ELEMENTS, BY EMISSION SPECTROSCOPY, IN THE WATER-SOLUBLE* AND WATER-INSOLUBLE* PORTIONS OF "BeO EXHAUST PRODUCT"

	Percent (%) of:	
Element	Water-Soluble Fraction	Water-Insoluble Fraction
Al	0.0001	0.004
As	<0.00005	--
Ba	<0.00001	<0.001
Bi	<0.000005	--
B	--	0.001-0.01
Ca	0.0046	0.4
Cd	<0.00001	<0.01
Co	<0.0000005	<0.001
Cu	<0.0000001	0.001
Cr	0.0001	0.05
Fe	0.00005	0.08
In	<0.000001	--
K	<0.0005	--
Li	<0.000005	--
Mg	0.0002	0.3
Mn	<0.0000001	0.005
Mo	0.0000007	<0.001
Ni	<0.0000005	0.006
P	<0.0001	<0.05
Pb	<0.000001	~0.001
Ag	<0.0000001	--
Si	0.0063	0.4
Sn	0.000005	~0.001
Sb	<0.00001	--
Sr	<0.00005	<0.001
Na	--	0.01-0.1
Ti	<0.0000002	0.1
V	<0.000005	<0.001
Zn	<0.00005	0.01-0.1
Zr	<0.000002	--

*After 16 hours of shaking a 1% suspension in water, at room temperature, and filtration through a 0.45μ Millipore filter.

TABLE V

SOLUBLE BERYLLIUM IN "BeO EXHAUST PRODUCT"

Solvent	Soluble Beryllium, % in Original Sample*
H_2O	0.0004
0.1 N HCl	0.0108
6 N HCl	0.0009

* Determined by emission spectroscopy

TABLE VI

BERYLLIUM, CHLORINE, CARBON, HYDROGEN AND OXYGEN ANALYSES ON "BeO EXHAUST PRODUCT"

Element	Percent (% in Total Sample
Be	34.6 $\pm$ 0.2
Cl	0.03 - 0.04
C	0.40 $\pm$ 0.03
H	0.11 $\pm$ 0.01
O	62.6 $\pm$ 2.0

TABLE VII

COULTER COUNTER DETERMINATION OF PARTICLE SIZE DISTRIBUTION OF "BeO EXHAUST PRODUCT"

Particle Size Range	% of Mass of Particles in Sample
< 1.5μ	0.5
1.5 - 5.04μ	29.04
5.04 - 10.8μ	57.55
> 10.8μ	12.89

TABLE VIII

EXPERIMENTAL DESIGN FOR FEMALE RATS RECEIVING "BeO EXHAUST PRODUCT"

BY INTRATRACHEAL ADMINISTRATION

Sample	Dose mg/kg	No. of Rats Treated	Number of Rats Scheduled for Necropsy			
			25 Weeks	50 Weeks	75 Weeks	100 Weeks
"BeO Exhaust Product"	50	60	10	10	10	All Survivors
	10	60	10	10	10	All Survivors
	2	60	10	10	10	All Survivors
BeO Calcined at 500 C	50	60	10	10	10	All Survivors
Saline Control	0	60	10	10	10	All Survivors
TOTAL		300	50	50	50	

TABLE IX

SUMMARY OF MORTALITY OF GROUPS OF FEMALE RATS DURING A 100-WEEK PERIOD FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Sample and Dose	No. of Deaths/No. in Group*
"BeO Exhaust Product"	
50 mg/kg	20/30
10 mg/kg	15/30
2 mg/kg	22/30
BeO Calcined at 500 C	
50 mg/kg	25/30
Saline Control	19/30

* Does not include the 30 rats/group killed at various scheduled interim necropsies

TABLE X

TERMINAL BODY AND ORGAN WEIGHTS OF FEMALE RATS KILLED 25 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"*

Sample and Dose	No. of Rats	Avg Body Wt. (g)	Heart		Liver		Kidney		Spleen		Brain	
			g	g/100 g	g	g/100 g	g	g/100 g	g	g/100 g	g	g/100 g
"BeO Exhaust Product"												
50 mg/kg	10	328 ± 20	1.17 ± 0.13	0.36 ± 0.04	8.38 ± 0.85	2.56 ± 0.24	2.44 ± 0.21	0.75 ± 0.08	0.64 ± 0.08	0.20 ± 0.02	1.75 ± 0.07	0.54 ± 0.03
10 mg/kg	10	308 ± 18	1.12 ± 0.08	0.36 ± 0.02	8.15 ± 0.97	2.65 ± 0.26	2.46 ± 0.32	0.80 ± 0.10	0.63 ± 0.07	0.21 ± 0.03	1.70 ± 0.02	0.56 ± 0.03
2 mg/kg	10	321 ± 18	1.12 ± 0.14	0.35 ± 0.05	7.84 ± 0.73	2.44 ± 0.19	2.37 ± 0.21	0.74 ± 0.08	0.61 ± 0.05	0.19 ± 0.02	1.76 ± 0.07	0.55 ± 0.04
BeO Calcined at 500 C												
50 mg/kg	10	312 ± 19	1.12 ± 0.15	0.36 ± 0.04	7.51 ± 0.81	2.40 ± 0.14	2.19 ± 0.19	0.70 ± 0.03	0.62 ± 0.08	0.20 ± 0.02	1.72 ± 0.05	0.55 ± 0.04
Saline Control	10	322 ± 24	1.09 ± 0.12	0.34 ± 0.05	8.18 ± 0.84	2.55 ± 0.21	2.39 ± 0.31	0.74 ± 0.09	0.64 ± 0.09	0.20 ± 0.02	1.72 ± 0.06	0.54 ± 0.04

*No significant difference between control and treatment groups (Student's t test)

TABLE XI

TERMINAL BODY AND ORGAN WEIGHTS OF FEMALE RATS KILLED 50 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"[1]

Sample and Dose	Avg. Body Wt. (g)	Heart		Liver		Kidney		Spleen		Brain	
		g	g/100 g	g	g/100 g	g	g/100 g	g	g/100 g	g	g/100 g
"BeO Exhaust Product"											
50 mg/kg	340 ± 33	1.12 ± 0.10	0.33 ± 0.03	8.11 ± 1.08	2.39 ± 0.30	2.51 ± 0.43	0.75 ± 0.14	0.62 ± 0.09	0.18 ± 0.03	1.68 ± 0.08*	0.50 ± 0.03
10 mg/kg	365 ± 57	1.31 ± 0.15	0.36 ± 0.04	9.58 ± 1.71	2.65 ± 0.51	2.89 ± 0.88	0.81 ± 0.30	0.66 ± 0.08	0.18 ± 0.02	1.70 ± 0.16	0.47 ± 0.08
2 mg/kg	356 ± 24	1.20 ± 0.09	0.34 ± 0.03	8.65 ± 1.40	2.43 ± 0.39	2.69 ± 0.36	0.76 ± 0.10	0.64 ± 0.12	0.18 ± 0.03	1.77 ± 0.06	0.50 ± 0.04
BeO Calcined at 500 C											
50 mg/kg	363 ± 27	1.23 ± 0.06	0.34 ± 0.03	8.53 ± 0.61	2.36 ± 0.17	2.40 ± 0.19	0.66 ± 0.06*	0.65 ± 0.08	0.18 ± 0.01	1.74 ± 0.07	0.48 ± 0.03
Saline Control	357 ± 29	1.22 ± 0.16	0.34 ± 0.03	8.89 ± 1.12	2.49 ± 0.21	2.62 ± 0.29	0.73 ± 0.07	0.68 ± 0.10	0.19 ± 0.02	1.77 ± 0.05	0.50 ± 0.05

[1]Mean ± standard deviation of 10 rats/dose

*P<0.05 (Student's t test)

TABLE XII

TERMINAL BODY AND ORGAN WEIGHTS OF FEMALE RATS KILLED 75 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EHAUST PRODUCT"[1]

Sample and Dose	Ave. Body Wt. (g)	Heart		Liver		Kidney		Spleen		Brain	
		g	g/100 g	g	g/100 g	g	g/100 g	g	g/100 g	g	g/100 g
"BeO Exhaust Product"											
50 mg/kg	349±37*	1.32±0.13	0.37±0.04	10.70±2.02	3.10±0.73	3.18±0.92	0.92±0.33	0.77±0.20	0.22±0.05	1.76±0.09	0.50±0.05*
10 mg/kg	432±73	1.25±0.12	0.29±0.06	13.28±2.58	3.08±0.45	3.04±0.29	0.72±0.14	0.79±0.18	0.18±0.06	1.71±0.10	0.40±0.07
2 mg/kg	386±44	1.26±0.15	0.32±0.02	10.59±1.74	2.64±0.24	3.01±0.33	0.78±0.11	0.79±0.38	0.19±0.07	1.78±0.08	0.46±0.05
BeO Calcined at 500 C -											
50 mg/kg	337±32*	1.19±0.11	0.35±0.04	9.44±0.99*	2.83±0.48	2.64±0.24*	0.78±0.11	0.71±0.17	0.21±0.06	1.75±0.10	0.52±0.05*
Saline Control	389±41	1.28±0.13	0.33±0.04	11.38±1.83	2.93±0.48	3.31±0.68	0.86±0.21	0.72±0.11	0.18±0.03	1.72±0.20	0.44±0.08

[1]Mean±standard deviation of 10 rats/dose

*P<0.05 (Student's t test)

TABLE XIII

TERMINAL BODY AND ORGAN WEIGHTS OF FEMALE RATS KILLED 100 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Sample and Dose	No. of Rats	Mean Body Wt. (g)	Heart		Liver		Kidney	
			g	g/100 g	g	g/100 g	g	g/100 g
"BeO Exhaust Product"								
50 mg/kg	10	385±52	1.28 ± 0.11	0.34 ± 0.06	12.32 ± 1.72	3.24 ± 0.66	3.08 ± 0.45	0.81 ± 0.15
10 mg/kg	15	374±52	1.36 ± 0.12	0.36 ± 0.05	11.57 ± 1.96	3.12 ± 0.60	3.21 ± 0.37	0.87 ± 0.19
2 mg/kg	8	411±59	1.49 ± 0.24	0.36 ± 0.08	12.52 ± 2.47	3.10 ± 0.83	3.38 ± 1.31	0.86 ± 0.46
BeO Calcined at 500 C								
50 mg/kg	5	340±60	1.43 ± 0.06	0.42 ± 0.06	12.27 ± 2.66	3.64 ± 0.60	3.15 ± 0.52	0.94 ± 0.19
Saline Control	11	383±72	1.36 ± 0.14	0.36 ± 0.06	12.95 ± 3.75	3.38 ± 0.70	3.43 ± 0.51	0.92 ± 0.22

TABLE XIII, (Cont'd)

Sample and Dose	No. of Rats	Mean Body Wt. (g)	Spleen		Brain	
			g	g/100 g	g	g/100 g
"BeO Exhaust Product"						
50 mg/kg	10	385 ± 52	0.81 ± 0.12	0.21 ± 0.04	1.81 ± 0.08	0.48 ± 0.07
10 mg/kg	15	374 ± 52	0.86 ± 0.36	0.23 ± 0.11	1.79 ± 0.05	0.48 ± 0.06
2 mg/kg	8	411 ± 59	0.90 ± 0.18	0.22 ± 0.03	1.71 ± 0.17	0.43 ± 0.08
BeO Calcined at 500 C						
50 mg/kg	5	340 ± 60	1.04 ± 0.17	0.31 ± 0.06*	1.80 ± 0.06	0.54 ± 0.09
Saline Control	11	383 ± 72	0.81 ± 0.25	0.21 ± 0.08	1.80 ± 0.05	0.47 ± 0.07

* $P < 0.05$ - Student's "t" test.

TABLE XIV

GROSS AND MICROSCOPIC CHANGES OBSERVED IN LUNGS AND ASSOCIATED LYMPH NODES IN FEMALE RATS EXAMINED 25 WEEKS AFTER SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
Control, Saline, 1 ml, 10 Rats Examined	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 9/10 Rats - no visible lesions. 1/10 Rats - one minimal focus of alveolar epithelialization.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - no visible lesions.
"BeO Exhaust Product," 50 mg/kg, 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 10/10 Rats - typical lung reaction included multifocal accumulation of intra-alveolar proteinaceous material, alveolar macrophages, polymorphonuclear leukocytes and translucent aggregates assumed to be test material. Multifocal areas of alveolar epithelialization consistently present in all rats. Squamous metaplasia with keratin formation in one rat and focal necrosis of alveolar walls in two rats.	GROSS: 9/10 Rats - no visible lesions. 1/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of test material, but no proliferative response.

TABLE XIV, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
"BeO Exhaust Product" 10 mg/kg 10 Rats Examined	GROSS: 5/10 Rats - no visible lesions. 5/10 Rats - multifocal areas of consolidation, minimal. MICROSCOPIC: 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, polymorphonuclear leukocytes and translucent aggregates assumed to be test material. Multifocal areas of alveolar epithelialization present in all rats. Above changes more focal and less severe than changes in higher dosage group.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - aggregates of test material, but no proliferative response.
"BeO Exhaust Product" 2 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - vast majority of lung normal. Typical lung reaction included accumulation of alveolar macrophages and translucent aggregates assumed to be test material. Minimal focal alveolar epithelialization present. Above changes all very minimal and focal.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - few aggregates of test material, but no proliferative response.

TABLE XIV, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
BeO Calcined at 500 C 50 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, polymorphonuclear leukocytes, translucent aggregates assumed to be the BeO test material, multifocal areas of alveolar epithelialization and necrosis of alveolar walls. Advanced squamous metaplasia and keratin formation in two rats and focal septal fibrosis in one rat.	GROSS: 10/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of BeO test material accompanied by a proliferative response, with deposition of fibrotic tissue.

TABLE XV

GROSS AND MICROSCOPIC CHANGES OBSERVED IN LUNGS AND ASSOCIATED LYMPH NODES IN FEMALE RATS EXAMINED 50 WEEKS AFTER SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
Control, Saline 1 ml 10 Rats Examined	GROSS: 10/10 Rats - No visible lesions. MICROSCOPIC: 10/10 Rats - no visible lesions.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - no visible lesions.
"BeO Exhaust Product" 50 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, and translucent aggregates assumed to be test material. Multifocal areas of alveolar epithelialization and squamous metaplasia with keratin formation observed in all rats.	GROSS: 2/10 Rats - no visible lesions. 8/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of test material, but no proliferative response.

TABLE XV, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
"BeO Exhaust Product" 10 mg/kg 10 Rats Examined	GROSS: 2/10 Rats - no visible lesions. 8/10 Rats - multifocal areas of consolidation, minimal. MICROSCOPIC: 10/10 Rats - typical lung reaction included multifocal accumulations of alveolar macrophages, translucent aggregates assumed to be test material and multifocal areas of alveolar epithelialization. Three rats with accumulations of intra-alveolar proteinaceous material and one rat with squamous metaplasia and keratin formation. Polymorphonuclear leukocytes present in one rat. Above changes more focal and less severe than changes in higher dosage group.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - aggregates of test material, but no proliferative response.
"BeO Exhaust Product" 2 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - vast majority of lung normal. Typical lung reaction included accumulations of alveolar macrophages and translucent aggregates assumed to be test material. Two rats also showing minimal accumulations of intra-alveolar proteinaceous material and focal alveolar epithelialization. All above changes minimal and focal.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - few aggregates of test material, but no proliferative response.

TABLE XV, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
BeO Calcined at 500 C 50 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, polymorphonuclear leukocytes, translucent aggregates assumed to be the test material multifocal alveolar epithelialization and squamous metaplasia with keratin formation. Two rats had focal septal fibrosis.	GROSS: 10/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of BeO test material accompanied by a proliferative response, with deposition of fibrotic tissue.

TABLE XVI

GROSS AND MICROSCOPIC CHANGES OBSERVED IN LUNGS AND ASSOCIATED LYMPH NODES IN FEMALE RATS EXAMINED 75 WEEKS AFTER SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

No. Rats Examined	Lungs	Associated Lymph Nodes
Control, Saline 1 ml 10 Rats Examined	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 7/10 Rats - no visible lesions. 3/10 Rats - several small foci of macrophages, lymphocytes and polymorphonuclear leukocytes in alveoli.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - no visible lesions.
"BeO Exhaust Product" 50 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 4/10 Rats - pulmonary carcinoma. 1/10 Rats - pulmonary adenoma. 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages and translucent aggregates assumed to be the test material. Multifocal areas of alveolar epithelialization and squamous metaplasia with keratin formation observed in all rats. Adenomatoid changes observed in four rats and focal septal fibrosis in one rat.	GROSS: 10/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of test material but no proliferative response.

TABLE XVI, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
"BeO Exhaust Product" 10 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation, minimal. MICROSCOPIC: 1/10 Rats - pulmonary carcinoma. 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages and translucent aggregates assumed to be the test material. Two rats had focal squamous metaplasia with keratin formation. Above changes more focal and less severe than changes in higher dosage group.	GROSS: 10/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of test material but no proliferative response.
"BeO Exhaust Product" 2 mg/kg 10 Rats Examined	GROSS: 6/10 Rats - no visible lesions. 4/10 Rats - focal areas of consolidation, minimal. MICROSCOPIC: 10/10 Rats - vast majority of lung normal. Typical lung reaction included focal accumulations of alveolar macrophages and translucent aggregates assumed to be test material. Four rats also show minimal focal accumulations of intra-alveolar proteinaceous material and scattered foci in alveolar epithelialization. All above changes minimal and focal.	GROSS: 10/10 Rats - no visible lesions. MICROSCOPIC: 10/10 Rats - rare to no aggregates of test mterial, with no proliferative response.

TABLE XVI, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
BeO Calcined at 500 C 50 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 5/10 Rats - pulmonary carcinoma. 1/10 Rats - pulmonary adenoma. 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages, translucent aggregates assumed to be test material, multifocal alveolar epithelialization, squamous metaplasia with keratin formation, septal fibrosis and areas of adenomatoid change.	GROSS: 10/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of BeO test material accompanied by a proliferative response, with deposition of fibrotic tissue.

TABLE XVII

GROSS AND MICROSCOPIC CHANGES OBSERVED IN LUNGS AND ASSOCIATED LYMPH NODES IN FEMALE RATS EXAMINED 100 WEEKS AFTER SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
Control, Saline 1 ml 11 Rats Examined	GROSS: 11/11 Rats - no visible lesions. MICROSCOPIC: 7/11 Rats - no visible lesions. 4/11 - very minimal accumulations of alveolar macrophages and proteinaceous material.	GROSS: 11/11 Rats - no visible lesions. MICROSCOPIC: 11/11 Rats - no visible lesions.
"BeO Exhaust Product" 50 mg/kg 10 Rats Examined	GROSS: 10/10 Rats - multifocal areas of consolidation. MICROSCOPIC: 9/10 Rats - pulmonary carcinoma. 10/10 Rats - typical lung reaction included multifocal accumulations of intra-alveolar macrophages and translucent aggregates assumed to be test material. Multifocal areas of alveolar metaplasia, visible as adenomatous and adenomatoid change associated with areas of septal fibrosis.	GROSS: 10/10 Rats - enlarged lymph nodes. MICROSCOPIC: 10/10 Rats - aggregates of test material but no proliferative response.

TABLE XVII, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
"BeO Exhaust Product" 10 mg/kg 15 Rats Examined	GROSS: 1/15 Rats - no visible lesions. 14/15 Rats - multifocal areas of consolidation, minimal. MICROSCOPIC: 15/15 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages and translucent aggregates assumed to be test material. Focal metaplasia of alveolar epithelium and focal septal fibrosis. One rat with a focus of massive mobilization of macrophages. Above changes more focal and less severe than changes observed in higher dosage group.	GROSS: 1/15 Rats - no visible lesions. 14/15 Rats - enlarged lymph nodes. MICROSCOPIC: 3/15 Rats - no visible lesions. 12/15 Rats - aggregates of test material, but no proliferative response.
"BeO Exhaust Product" 2 mg/kg 8 Rats Examined	GROSS: 6/8 Rats - no visible lesions. 2/8 Rats - focal areas of consolidation, minimal. MICROSCOPIC: 8/8 Rats - vast majority of lung normal. Typical lung reaction, included focal accumulations of intra-alveolar proteinaceous material, alveolar macrophages and translucent aggregates assumed to be test material. Minimal focal septal fibrosis occasionally present. One rat showing one isolated focus of squamous metaplasia. All above changes minimal and focal.	GROSS: 8/8 Rats - no visible lesions. MICROSCOPIC: 8/8 Rats - rare to no aggregates of test material, with no proliferative response.

TABLE XVII, continued

Treatment and No. Rats Examined	Lungs	Associated Lymph Nodes
BeO Calcined at 500 C 50 mg/kg 5 Rats Examined	GROSS: 5/5 Rats - multifocal areas of consolidation. MICROSCOPIC: 5/5 Rats - pulmonary carcinoma. 5/5 Rats - typical lung reaction included multifocal accumulations of intra-alveolar proteinaceous material, alveolar macrophages and translucent aggregates assumed to be test material. Multifocal areas of alveolar metaplasia visible as adenomatous and adenomatoid change associated with areas of septal fibrosis.	GROSS: 5/5 Rats - enlarged lymph nodes. MICROSCOPIC: 5/5 Rats - aggregates of BeO test material accompanied by proliferative response, with deposition of fibrotic tissue. 2/5 Rats - metastatic carcinoma cells present.

TABLE XVIII

LESIONS OBSERVED DURING GROSS AND MICROSCOPIC EXAMINATION OF NON-PULMONARY MAJOR ORGANS OF FEMALE RATS 100 WEEKS AFTER SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT" (Excluding Tumors Listed Separately in Table XIX)

Lesions Noted (gross and microscopic)	Saline (Control) 11 Rats	BeO Calcined 500 C (50 mg/kg) 5 Rats	"Beo Exhaust Product" 50 mg/kg 10 Rats	10 mg/kg 15 Rats	2 mg/kg 8 Rats
LIVER - Biliary cyst formation, minimal	0/11	0/5	0/10	3/15	0/8
Focal hepatitis, minimal	0/11	0/5	0/10	1/15	0/8
Dilatation and congestion of sinusoids	8/11	2/5	4/10	7/15	5/8
Hepatocellular hyperplastic nodule	0/11	1/5	0/10	0/15	0/8
Focal area of fatty change	0/11	0/5	0/10	3/15	0/8
HEART - Fibrotic pericarditis	0/11	0/5	0/10	0/15	1/8
Focal myocardial degeneration	5/11	3/5	7/10	5/15	1/8
SPLEEN - Major increase in hemopoiesis	1/11	0/5	0/10	1/15	0/8
Metastic proliferation, fibrosarcoma	0/11	0/5	0/10	0/15	1/8

TABLE XIX

NON-PULMONARY TUMORS AND TUMOR-LIKE LESIONS OBSERVED IN FEMALE RATS EXAMINED 100 WEEKS AFTER SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Saline (Control)	Mammary Fibroadenoma	10/11 Rats
	Pituitary Adenoma	10/11 Rats
	Uterine Polyp Formation	7/11 Rats
	Mesenteric Lipoma	1/11 Rats
BeO Calcined at 500 C (50 mg/kg)	Mammary Fibroadenoma	5/5 Rats
	Pituitary Adenoma	4/5 Rats
"BeO Exhaust Product" (50 mg/kg)	Mammary Fibroadenoma	5/10 Rats
	Pituitary Adenoma	6/10 Rats
	Lymphoma of Thymus	1/10 Rats
	Cholangioma	1/10 Rats
"BeO Exhaust Product" (10 mg/kg)	Mammary Fibroadenoma	7/15 Rats
	Mammary Adenocarcinoma	1/15 Rats
	Pituitary Adenoma	13/15 Rats
	Uterine Polyp	2/15 Rats
	Thyroid Adenoma	2/15 Rats
	Adrenal Cortical Adenoma	1/15 Rats
"BeO Exhaust Product" (2 mg/kg)	Mammary Fibroadenoma	4/8 Rats
	Mammary Adenocarcinoma	1/8 Rats
	Pituitary Adenoma	3/8 Rats
	Lipoma of Kidney	1/8 Rats
	Uterine Polyp	3/8 Rats
	Thyroid Adenoma	1/8 Rats
	Vaginal Myxoma	1/8 Rats
	Fibrosarcoma	1/8 Rats

TABLE XX

MAJOR LESIONS NOTED AT GROSS AND MICROSCOPIC EXAMINATION OF FEMALE RATS DYING DURING COURSE OF 100 WEEK OBSERVATION PERIOD FOLLOWING SINGLE INTRATRACHEAL ADMINISTRATION OF SALINE (Control Group)

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2384	57	Spontaneous death; evidence of acute pneumonic inflammation in lungs.
70-2371	463	Spontaneous death; severe autolysis precluded definitive examination.
70-2342	496	Spontaneous death; mammary fibroadenoma, focal myocardial degeneration, minimal chronic nephritis, with mineralized deposits.
70-2350	532	Spontaneous death; pituitary adenoma, severe mesenteric vessel periarteritis and sclerosis, minimal chronic nephritis with mineralized deposits.
70-2361	532	Spontaneous death; mammary fibroadenoma, severe chronic nephritis, diffuse fatty change in liver.
70-2366	534	Moribund; large mammary fibroadenoma, minimal chronic nephritis.
70-2367	568	Moribund; pituitary adenoma, severe chronic nephritis, mammary fibroadenoma.

TABLE XX, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2351	574	Spontaneous death; pituitary adenoma, focal myocardial degeneration, minimal chronic nephritis.
70-2341	584	Spontaneous death; hepatic tumor (hepatocellular carcinoma) focal myocardial degeneration.
70-2357	604	Moribund; large mammary fibroadenoma, minimal chronic nephritis.
70-2365	604	Moribund; large mammary fibroadenoma, moderate chronic nephritis, pituitary adenoma.
70-2343	604	Moribund; large mammary fibroadenoma, moderate chronic nephritis.
70-2363	611	Spontaneous death; adrenal cortical tumor (adenoma), enlarged pituitary (adenoma), moderate chronic nephritis, galactocele.
70-2356	614	Spontaneous death; pituitary adenoma, moderate chronic nephritis.
70-2362	619	Moribund; large mammary fibroadenoma, minimal chronic nephritis.

TABLE XX, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2355	628	Moribund; undifferentiated sarcoma of uterus, mammary adenoma, pituitary adenoma.
70-2349	648	Moribund; large mammary fibroadenoma, hepatocyte vacuolization, moderate chronic nephritis, pituitary adenoma.
70-2344	667	Spontaneous death; adrenal cortical adenoma, mammary fibroadenoma, moderate chronic nephritis.
70-2354	687	Moribund; severe chronic nephritis, focal myocardial degeneration, pituitary adenoma, fatty change in liver, increased number alveolar macrophages in lung, mesenteric vessel sclerosis.

TABLE XXI

MAJOR LESIONS NOTED AT GROSS AND MICROSCOPIC EXAMINATION OF FEMALE RATS DYING DURING COURSE OF 100 WEEK OBSERVATION PERIOD FOLLOWING SINGLE INTRATRACHEAL ADMINISTRATION OF 50 MG/KG OF "BeO EXHAUST PRODUCT"

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2166	308	Moribund; large mammary fibroadenoma, lung contains test material aggregates, accompanied by intra-alveolar macrophages, other inflammatory cells and material. Minimal to moderate alveolar hyperplasia, aggregates in mediastinal lymph nodes.
70-2196	350	Moribund; large mammary fibroadenoma, lung contains test material aggregates, accompanied by alveolar macrophages, other inflammatory cells and material, minimal focal alveolar hyperplasia.
70-2163	484	Moribund; large mammary fibroadenoma, lung contains test material aggregates, accompanied by intra-alveolar macrophages plus other inflammatory cells and material, alveolar hyperplasia and thickening, minimal chronic nephritis, uterine polyp, aggregates in mediastinal lymph nodes.
70-2173	497	Moribund; large mammary fibroadenoma, lung contains test material aggregates accompanied by intra-alveolar macrophages plus other inflammatory cells and material, minimal hyperplasia and metaplasia in alveoli and bronchioles, minimal chronic nephritis.

TABLE XXI, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2181	534	Moribund; pulmonary carcinoma, with metastasis to lymph nodes and kidney, multifocal proliferative pneumonitis near test material aggregates, with changes extending into plasia and adenomatosis, uterine polyp.
70-2175	538	Spontaneous death; large mammary fibroadenoma, severe chronic nephritis, focal myocardial degeneration, test material aggregates in lung, accompanied by proliferative response extending into metaplasia and adenomatosis.
70-2177	555	Moribund; large mammary fibroadenoma, multifocal proliferative pneumonitis near test material aggregates, with changes extending into metaplasia and adenomatosis, aggregates in mediastinal lymph nodes, minimal chronic nephritis, pituitary adenoma.
70-2172	567	Moribund; pituitary adenoma, test material aggregates in lung accompanied by inflammatory cells and material, with changes extending into alveolar hyperplasia, BeO aggregates in mediastinal lymph node, galactocele formation, focal myocardial degeneration, minimal chronic nephritis.
70-2165	579	Spontaneous death; pituitary adenoma, test material aggregates in lung, accompanied by inflammatory cells and material with focal changes extending into metaplasia, aggregates in mediastinal lymph nodes, minimal chronic nephritis.

TABLE XXI, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2179	600	Spontaneous death; pulmonary carcinoma, with test material aggregates accompanied by proliferative pneumonitis extending into metaplasia, pituitary adenoma, minimal chronic nephritis.
70-2176	604	Moribund; large mammary fibroadenoma, multifocal proliferative pneumonitis near test material aggregates, with changes extending into metaplasia and adenomatosis, adrenal hematocyst.
70-2160	604	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near test material aggregates with change extending into metaplasia and adenomatosis, large mammary fibroadenoma, pituitary adenoma, minimal chronic nephritis.
70-2161	604	Spontaneous death; pituitary adenoma, severe chronic nephritis, test material aggregates in lung, accompanied by inflammatory changes altered by autolysis (no tumor formation in lung).
70-2164	604	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near test material aggregates, with changes extending into metaplasia and adenomatosis, pituitary adenoma, mammary adenoma, moderate chronic nephritis.
70-2182	613	Spontaneous death; pituitary adenoma, autolysis precluded definitive examination of lung, but changes appeared to be of a non-tumorous proliferative reaction in lung.

TABLE XXI, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2188	619	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates, with changes extending into metaplasia and adenomatosis, large mammary fibroadenoma, very minimal chronic nephritis.
70-2187	619	Moribund; severe chronic nephritis, mammary fibroadenoma, pituitary adenoma, multifocal proliferative pneumonitis near aggregates, with changes extending into metaplasia and adenomatosis.
70-2170	619	Moribund; pituitary adenoma, mammary adenocarcinoma, minimal multifocal proliferative pneumonitis near aggregates, minimal chronic nephritis.
70-2169	619	Moribund; severe chronic nephritis, mammary fibroadenoma, mesenteric vessel sclerosis and periarteritis, focal myocardial degeneration, adrenal cortical adenoma and hematocyte formation, multifocal proliferative pneumonitis near aggregates, with changes extending into metaplasia and adenomatosis.
70-2168	628	Moribund; large mammary fibroadenoma, hepatocellular hyperplastic nodular formation, multifocal proliferative pneumonitis near aggregates, with changes extending into metaplasia and adenomatosis.

TABLE XXII

MAJOR LESIONS NOTED AT GROSS AND MICROSCOPIC EXAMINATION OF FEMALE RATS DYING DURING COURSE OF 100 WEEK OBSERVATION PERIOD FOLLOWING SINGLE INTRATRACHEAL ADMINISTRATION OF 10 MG/KG OF "BeO EXHAUST PRODUCT"

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2269	42	Spontaneous death; subcutaneous tumor, rhabdomyosarcoma, few aggregates in lung, accompanied by alveolar macrophages.
70-2257	401	Moribund; large mammary fibroadenoma, minimal chronic nephritis, minimal focal aggregates in lung, accompanied by minimal focal alveolar macrophages and inflammatory material, minimal focal peribronchiolar alveolar hyperplasia, minimal amounts of aggregates in mediastinal lymph nodes, pituitary adenoma.
70-2223	464	Moribund; pituitary adenoma, mammary fibroadenoma, minimal focal aggregates in lung accompanied by minimal focal alveolar marcrophages, inflammatory material and slight thickening of adjacent alveolar walls, aggregates in mediastinal lymph nodes, moderate chronic nephritis.
70-2222	474	Spontaneous death; autolysis advanced, some microscopic evidence of severe chronic nephritis, no evidence of pulmonary tumor.
70-2227	484	Moribund; large mammary fibroadenoma, reaction in lung limited to very slight increase in intra-alveolar macrophages and slight thickening of alveolar walls adjacent to aggregates, pituitary adenoma, minimal chronic nephritis

TABLE XXII, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2237	484	Moribund; severe chronic nephritis, galactocele formation with adjacent cellulitis, few minimal aggregates in lung accompanied by minimal focal alveolar macrophages and slight thickening of adjacent alveolar walls.
70-2233	506	Spontaneous death; pituitary adenoma, advanced autolysis but no gross or microscopic evidence of pulmonary tumor.
70-2247	583	Moribund; pituitary adenoma, minimal chronic nephritis, few aggregates in lung accompanied by minimal alveolar macrophages and inflammatory material.
70-2221	584	Spontaneous death; severe chronic nephritis with abscessation, focal myocardial degeneration, adrenal hematocyst, mammary fibroadenoma, few aggregates in lung accompanied by minimal focal alveolar macrophages and inflammatory material.
70-2245	604	Moribund; pituitary adenoma, mammary fibroadenoma, moderate chronic nephritis, minimal aggregates in lung accompanied by minimal alveolar macrophages and inflammatory material, mesenteric vessel sclerosis and periarteritis.

TABLE XXII, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2234	615	Moribund; severe chronic nephritis, adrenal hematocyst, mammary galactocele, few aggregates in lung, accompanied by minimal alveolar macrophages and inflammatory material, acute bronchopneumonitis also present.
70-2243	628	Spontaneous death; moderate chronic nephritis, few aggregates in lung accompanied by minimal focal alveolar macrophages, autolysis advanced.
70-2244	628	Moribund; large mammary fibroadenoma, minimal chronic nephritis few aggregates in lung, accompanied by few alveolar macrophages, inflammatory material and minimal focal thickening and hyperplasia of adjacent alveolar walls.
70-2246	643	Moribund; pituitary adenoma, moderate chronic nephritis, few aggregates in lung accompanied by minimal alveolar macrophages, inflammatory material, and slight thickening of adjacent alveolar walls.
70-2242	648	Moribund; pituitary adenoma, mammary fibroma, moderate chronic nephritis and pyelitis, few aggregates in lung accompanied by minimal alveolar macrophages and inflammatory material.

TABLE XXIII

MAJOR LESIONS NOTED AT GROSS AND MICROSCOPIC EXAMINATION OF FEMALE RATS DYING DURING COURSE OF 100 WEEK OBSERVATION PERIOD FOLLOWING SINGLE INTRATRACHEAL ADMINISTRATION OF 2 MG/KG OF "BeO EXHAUST PRODUCT"

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2312	224	Moribund; mammary fibroadenoma, minimal focal aggregates accompanied by minimal focal alveolar macrophages plus other inflammatory cells and material in alveoli, minimal amounts of aggregates in mediastinal lymph nodes.
70-2287	292	Spontaneous death; mammary adenocarcinoma, with metastasis to lungs, autolysis present.
70-2294	420	Spontaneous death; undifferentiated sarcoma, abdominal cavity, autolysis precluded definitive examination of the other organs, but no evidence of pulmonary tumor.
70-2310	420	Spontaneous death; overgrowth of incisor teeth, large mammary fibroadenoma, minimal chronic nephritis, minimal focal aggregates in lung accompanied by minimal focal alveolar macrophages and inflammatory material in alveoli.
70-2305	464	Moribund; large mammary fibroadenoma, moderate chronic nephritis, minimal focal aggregates in lung accompanied by minimal focal alveolar macrophages, inflammatory material and slight thickening of adjacent alveolar walls, pituitary adenoma.

TABLE XXIII, continued

Animal Number	Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2285	477	Moribund; pituitary adenoma, minimal focal aggregates of in lung accompanied by minimal focal alveolar macrophages, minimal chronic nephritis.
70-2306	534	Moribund; pituitary adenoma, large mammary fibroadenoma, minimal chronic nephritis, uterine adenoma, few aggregates in lung, accompanied by minimal alveolar macrophages and minimal hypercellularity of adjacent alveolar wall.
70-2283	600	Spontaneous death; pituitary adenoma, mammary fibroadenoma, autolysis advanced, but examination of lung revealed no evidence of proliferative response or tumor.
70-2280	602	Spontaneous death; mammary fibroadenocarcinoma, with metastasis to lung, no evidence of primary lung tumor formation, focal myocardial degeneration, moderate chronic nephritis.
70-2284	604	Moribund; pituitary adenoma, large mammary fibroadenoma, minimal chronic nephritis, few aggregates in lung, accompanied by minimal alveolar macrophages and minimal hypercellurity of adjacent alveolar wall.

TABLE XXIII, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2301	604	Moribund; large mammary fibroadenoma, minimal chronic nephritis, adrenal hematocyst, few aggregates in lung accompanied by minimal alveolar macrophages and minimal inflammatory material in alveolar.
70-2300	608	Spontaneous death; pituitary adenoma, large mammary fibroadenoma, severe chronic nephritis, adrenal hematocyst, focal myocardial degeneration, autolysis present, but examination of lung revealed no proliferative response or tumor formation.
70-2298	619	Moribund; large mammary fibroadenoma, minimal chronic nephritis, few aggregates in lung, accompanied by minimal hypercellularity of adjacent alveolar wall.
70-2289	619	Moribund; large mammary fibroadenoma, minimal chronic nephritis, sections of lung examined showed no visible lesions.
70-2307	619	Moribund; large mammary fibroadenoma,pituitary adenoma, minimal chronic nephritis, with cyst formation, few aggregates in lung accompanied by minimal alveolar macrophage and hypercellularity of adjacent alveolar wall.

TABLE XXIII, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2288	635	Moribund; severe chronic nephritis, pituitary adenoma, mammary galactocele, focal exudative and interstitial pneumonitis, possibly of infectious nature.
70-2303	648	Moribund; pituitary adenoma, severe chronic nephritis, mammary adenoma, few aggregates in lung, accompanied by alveolar macrophages and focal thickening of adjacent alveolar walls.
70-2282	648	Moribund; pituitary adenoma, severe chronic nephritis, aggregates in lung, accompanied by focal hyperplasia and squamous metaplasia, fibrosis, alveolar macrophages and inflammatory material.
70-2292	657	Moribund; severe chronic nephritis, undifferentiated sarcoma in mediastinum, with metastatic thrombosis and metastatic nodules in lung, few isolated aggregates in lung accompanied by minimal number of alveolar macrophages but no evidence of primary pulmonary proliferative response or tumor formation.
70-2304	657	Moribund; pituitary adenoma, large mammary fibroadenoma, moderate chronic nephritis, few aggregates in lung, accompanied by minimal alveolar macrophages plus focal hypercellularity and thickening of adjacent alveolar walls.

TABLE XXIII, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2299	663	Moribund; severe chronic nephritis, mesenteric vessel sclerosis and periarteritis, mammary fibroadenoma, ovarian cyst, focal aggregates in lung accompanied by alveolar macrophages and inflammatory material.
70-2302	675	Spontaneous death; pituitary adenoma, adrenal cortical tumor (adenoma), mammary fibroadenoma, lung showed no evidence of proliferative response or tumor formation (autolysis present).

TABLE XVIII, continued

Lesions Noted (gross and microscopic)	Saline (Control) 11 Rats	BeO Calcined 500 C (50 mg/kg) 5 Rats	"BeO Exhaust Product" 50 mg/kg 10 Rats	10 mg/kg 15 Rats	2 mg/kg 8 Rats
KIDNEY - Chronic nephritis, minimal	6/11	1/5	5/10	5/15	5/8
Chronic nephritis, moderate	5/11	2/5	4/10	8/15	2/8
Chronic nephritis, severe	0/11	2/5	1/10	2/15	1/8
Dilated renal pelvis, with calculi	2/11	0/5	1/10	2/15	0/8
OTHER - Focal cytoplasmic vacuolization, adrenal	0/11	0/5	0/10	0/15	1/8
Lymphoid hyperplasia, thymus	0/11	0/5	0/10	1/15	0/8
Thyroid hyperplasia	0/11	0/5	0/10	1/15	0/8
Hematocyst formation, adrenal	2/11	0/5	1/10	0/15	1/8
Parathyroid hyperplasia	1/11	0/5	0/10	0/15	0/8
Mesenteric periarteritis, sclerosis	1/11	0/5	2/10	1/15	0/8

Data listed as number of rats affected/number of rats examined.

TABLE XXIV

MAJOR LESIONS NOTED AT GROSS AND MICROSCOPIC EXAMINATION OF FEMALE RATS DYING DURING COURSE OF 100 WEEK OBSERVATION PERIOD FOLLOWING SINGLE INTRATRACHEAL ADMINISTRATION OF 50 MG/KG OF BeO CALCINED AT 500 C

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2408	213	Moribund; adenocarcinoma of mammary gland; multifocal proliferative pneumonitis near aggregates, with metaplasia and adenomatosis, minimal chronic nephritis.
70-2417	375	Spontaneous death; intra-abdominal sarcoma, with metastasis to lungs, multifocal proliferative pneumonitis near aggregates, with changes extending into metaplasia and adenomatosis, dilated renal pelvis.
70-2420	401	Moribund; mammary fibroadenoma, multifocal proliferative pneumonitis near aggregates, with changes extending to metaplasia and adenomatosis, aggregates in mediastinal lymph nodes, minimal chronic nephritis.
70-2423	401	Moribund; pulmonary adenocarcinoma, multifocal proliferative pneumonitis near aggregates with changes extending to metaplasia and adenomatosis, mammary adenocarcinoma, focal hepatitis.
70-2414	404	Spontaneous death; severe chronic nephritis, multifocal proliferative pneumonitis near aggregates, with changes extending to metaplasia and adenomatosis, thyroid adenoma, focal myocardial degeneration.

TABLE XXIV, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2404	435	Moribund; pituitary adenoma, multifocal proliferative pneumonitis near aggregates, with changes extending to metaplasia, adrenal hemangiectasis, minimal chronic nephritis.
70-2412	449	Spontaneous death; mammary adenoma; multifocal proliferative pneumonitis near aggregates.
70-2405	464	Moribund; pulmonary adenocarcinoma, multifocal proliferative pneumonitis near aggregates with changes extending to metaplasia and adenomatosis, severe chronic nephritis, mesenteric vessel periarteritis, particles and proliferative response in mediastinal lymph nodes, mammary fibroadenoma.
70-2427	477	Moribund; ptiuitary adenoma, multifocal proliferative pneumonitis near aggregates, with changes extending to metaplasia and adenomatosis, aggregates and proliferative response in mediastinal lymph nodes, minimal chronic nephritis.
70-2436	509	Spontaneous death; pulmonary adenocarcinoma, multifocal proliferative penumonitis near aggregates with changes to metaplasia and adenomatosis, advanced autolysis.
70-2437	512	Moribund; large mammary fibroadenoma, multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, minimal chronic nephritis, pituitary adenoma.

TABLE XXIV, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2415	532	Moribund pulmonary carcinoma, multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates and proliferative response and metastatic carcinoma cells in mediastinal lymph nodes, pituitary adenoma, minimal chronic nephritis.
70-2413	549	Spontaneous death; severe autolysis, some evidence of proliferative pneumonitis with squamous metaplasia and other changes.
70-2401	555	Moribund; pulmonary carcinoma, multifocal proliferative pneumonitis near aggregates with changes extending to metaplasia and adenomatosis, aggregates and proliferative response in mediastinal lymph nodes, minimal chronic nephritis.
70-2416	565	Spontaneous death; large intra-abdominal mass (undifferentiated sarcoma), multifocal proliferative pneumonitis near aggregates, with changes extending into adenomatosis, advanced autolysis.
70-2418	580	Spontaneous death; large mammary fibroadenoma, multifocal proliferative pneumonitis near aggregates, with changes extending into metaplasia and adenomatosis, aggregates and proliferative response in mediastinal lymph nodes, mesenteric vessel periarteritis.

TABLE XXIV, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2419	604	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, mediastinal lymph nodes with metastatic carcinoma and aggregates, subcutaneous galactocele, minimal chronic nephritis, pituitary adenoma, uterine polyp.
70-2426	604	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates in mediastinal lymph nodes, large mammary fibroadenoma, moderate chronic nephritis, focal myocardial degeneration, pituitary adenoma.
70-2422	604	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates and proliferative response in mediastinal lymph nodes, mammary fibroadenoma, minimal chronic nephritis.
70-2400	604	Muribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates in mediastinal lymph nodes, mammary fibroadenoma, uterine polyp, pituitary adenoma.

TABLE XXIV, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2411	619	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates in mediastinal lymph nodes, pituitary adenoma, mammary fibroadenoma, moderate chronic nephritis.
70-2409	628	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates and metastatic carcinoma in mediastinal lymph nodes, uterine polyp, pituitary adenoma, adrenal hematocyst.
70-2410	657	Moribund; pulmonary adenocarcinoma, with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates and proliferative response in mediastinal lymph nodes, pituitary adenoma, adrenal hematocyst, mammary adeno-fibrosarcoma, with metastasis to liver, spleen and heart, minimal chronic nephritis.
70-2402	663	Moribund; pulmonary adenocarcinoma wtih multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates and carcinoma metastasis in mediastinal lymph nodes, islet cell tumor of pancreas, pituitary adenoma, moderate chronic nephritis.

TABLE XXIV, continued

Animal Number	Time of Death (day)	Major Lesions Noted at Gross and Microscopic Examination
70-2403	685	Moribund; pulmonary adenocarcinoma with multifocal proliferative pneumonitis near aggregates with changes extending into metaplasia and adenomatosis, aggregates and carcinoma metastasis in mediastinal lymph nodes, pituitary adenoma, mammary fibroadenoma, focal myocardial degeneration, moderate chronic nephritis.

TABLE XXV

PRIMARY PULMONARY TUMORS IN RATS FOLLOWING INTRATRACHEAL ADMINISTRATION OF 50 mg/kg BeO CALCINED AT 500 C

	At Weekly Intervals			Cumulative Totals		
Weeks on Expt.	No. Rats Examined	No. Rats With Tumors	% Rats With Tumors	No. Rats Examined	No. Rats With Tumors	% Rats With Tumors
58	1	1	100	1	1	100
67	4	1	25	5	2	40
73	2	1	50	7	3	43
75	10	6	60	17	9	53
80	4	2	50	21	11	52
86	2	0	0	23	11	48
87	4	4	100	27	15	56
89	1	1	100	28	16	57
93	2	2	100	30	18	60
95	1	1	100	31	19	61
98	1	1	100	32	20	62
100	5	5	100	37	25	68

TABLE XXVI

PRIMARY PULMONARY TUMORS IN RATS FOLLOWING INTRATRACHEAL ADMINISTRATION OF 50 mg/kg "BeO EXHAUST PRODUCT"

	At Weekly Intervals			Cumulative Totals		
Weeks on Expt.	No. Rats Examined	No. Rats With Tumors	% Rats With Tumors	No. Rats Examined	No. Rats With Tumors	% Rats With Tumors
58	1	0	0	1	0	0
73	2	0	0	3	0	0
75	10	5	50	13	5	38
80	3	1	33	16	6	38
86	3	1	33	19	7	37
87	4	2	50	23	9	39
89	5	1	20	28	10	36
93	1	0	0	29	10	35
100	10	9	90	39	19	49

TABLE XXVII

PRIMARY PULMONARY TUMORS IN RATS FOLLOWING INTRATRACHEAL ADMINISTRATION OF 10 mg/kg "BeO EXHAUST PRODUCT"

	At Weekly Intervals			Cumulative Totals		
Weeks on Expt.	No. Rats Examined	No. Rats with Tumors	% Rats with Tumors	No. Rats Examined	No. Rats with Tumors	% Rats with Tumors
58	1	0	0	1	0	0
67	1	0	0	2	0	0
73	4	0	0	6	0	0
75	10	1	10	16	1	6
86	2	0	0	18	1	6
87	1	0	0	19	1	5
89	1	0	0	20	1	5
93	4	0	0	24	1	4
100	15	0	0	39	1	3

TABLE XXVIII

SUMMATION OF ALL PULMONARY TUMORS OCCURRING IN GROUPS OF FEMALE RATS FOLLOWING SINGLE INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Test Material Administered	75 Week Kill			100 Week Kill			Spontaneous Deaths			Totals*		
	Total No. Rats Examined	Number Rats with Primary Pulmonary Carcinoma	Number Rats with Primary Pulmonary Adenoma	Total No. Rats Examined	Number Rats with Primary Pulmonary Carcinoma	Number Rats with Primary Pulmonary Adenoma	Total No. Rats Examined	Number Rats with Primary Pulmonary Carcinoma	Number Rats with Primary Pulmonary Adenoma	Total No. Rats Examined	Number Rats with Primary Pulmonary Carcinoma	Number Rats with Primary Pulmonary Adenoma
Control, Saline, 1 ml	10	0/10	0/10	11	0/11	0/11	19	0/19	0/19	40	0/40	0/40
"BeO Exhaust Product," 50 mg/kg	10	4/10	1/10	10	9/10	0/10	20	5/20	0/20	40	18/40	1/40
"BeO Exhaust Product," 10 mg/kg	10	1/10	0/10	15	0/15	0/15	15	0/15	0/15	40	1/40	0/40
"BeO Exhaust Product," 2 mg/kg	10	0/10	0/10	8	0/8	0/8	22	0/22	0/22	40	0/40	0/40
BeO Calcined at 500 C, 50 mg/kg	10	5/10	1/10	5	5/5	0/5	25	14/25	0/25	40	24/40	1/40

*Excluding additional 20 rats/group, 10 of which were necropsied at 25 and at 50 weeks, respectively. No primary pulmonary tumors noted in any groups at these early necropsies.

TABLE XXIX

BERYLLIUM CONCENTRATION IN TISSUES OF RATS KILLED 25 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Sample	Dose mg/kg	Animal Number	Beryllium Concentration (µg/g tissue) Liver	Kidney	Spleen	Bone
"BeO Exhaust Product"	50	70-2210	1.7	0.01	1.7	0.52
		70-2211	0.07	0.01	0.09	0.45
		70-2212	0.16	0.01	0.26	0.47
		70-2213	0.07	0.01	0.10	0.31
	10	70-2270	<0.01	<0.01	0.03	<0.1
		70-2271	0.02	<0.01	0.04	<0.1
		70-2272	1.3	<0.01	0.84	<0.1
		70-2273	0.32	<0.01	0.40	<0.1
	2	70-2330	<0.01	<0.01	<0.01	<0.1
		70-2331	<0.01	<0.01	<0.01	<0.1
		70-2332	<0.01	<0.01	<0.01	<0.1
		70-2333	<0.01	<0.01	<0.01	<0.1
BeO Calcined at 500 C	50	70-2450	3.2	0.11	3.6	6.0
		70-2451	1.3	0.12	1.1	5.0
		70-2452	0.15	0.11	0.18	5.0
		70-2453	0.21	0.11	0.36	6.5
Saline Control	1 ml	70-2390	<0.01	<0.01	<0.01	<0.1
		70-2391	<0.01	<0.01	<0.01	<0.1
		70-2392	<0.01	<0.01	<0.01	<0.1
		70-2393	<0.01	<0.01	<0.01	<0.1

TABLE XXX

BERYLLIUM CONCENTRATION IN TISSUES OF RATS KILLED 100 WEEKS FOLLOWING INTRATRACHEAL ADMINISTRATION OF "BeO EXHAUST PRODUCT"

Sample	Dose mg/kg	Animal No.	Beryllium Concentration (µg/g Tissue) Liver	Kidney	Spleen	Bone
"BeO Exhaust Product"	50	70-2167	0.26	0.02	1.0	0.51
		70-2174	11.0	0.04	34.0	1.3
		70-2180	1.2	0.03	0.89	0.49
		70-2184	0.22	0.02	0.44	0.51
	10	70-2224	1.5	<0.01	3.0	<0.1
		70-2226	0.07	<0.01	0.12	<0.1
		70-2229	0.02	<0.01	0.05	<0.1
		70-2231	0.15	<0.01	0.25	<0.1
	2	70-2286	0.01	<0.01	0.02	<0.1
		70-2291	0.01	<0.01	0.03	<0.1
		70-2295	1.4	<0.01	1.6	<0.1
		70-2297	0.002	<0.01	0.04	<0.1
BeO Calcined at 500 C	50	70-2406	0.11	0.15	0.39	3.2
		70-2407	0.46	0.27	1.3	5.7
		70-2424	0.24	0.20	0.97	5.2
		70-2425	1.4	0.30	7.9	8.5
Saline Control		70-2345	<0.01	<0.01	<0.01	<0.1
		70-2347	<0.01	<0.01	<0.01	<0.1
		70-2352	<0.01	<0.01	<0.01	<0.1
		70-2358	<0.01	<0.01	<0.01	<0.1

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REFERENCES

(1) Spencer, H. C., R. H. Hook, J. A. Blumenshine, S. B. McCollister, S. E. Sadek, and J. C. Jones, Toxicological Studies on Beryllium Oxides and Beryllium-Containing Exhaust Products, AMRL-TR-68-148, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, December 1968.

(2) Gross, Paul, "A Self-Retaining Illuminated Laryngoscopic Speculum for Intratracheal Procedures," A.M.A. Arch. Ind. Health, 18, 429-430 1958.

(3) Cotchin, E., and F. C. Roe, Pathology of Laboratory Rats and Mice. Blackwell Publications, Oxford, 1967.

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